EPA Registration Jacket 82076-1
Vol.1

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Antimicrobials Division (7510C)
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

EPA Reg. Number: 82076-1

Date of Issuance: DEC 22 2005

Term of Issuance: UNCONDITIONAL

Name of Pesticide Product: MICROL Preservative

NOTICE OF PESTICIDE:
_x_ Registration
_____ Reregistration
(under FIFRA, as amended)

Name and Address of Registrant (include ZIP Code):

Petro Canada
Specialty Products and Fluids
2489 North Sheridan Way
Mississauga, Ontario L5K 1A8 CANADA

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is registered in accordance with FIFRA sec. 3(c)(5) and is subject to the following terms and conditions:

1. This registration does not eliminate the need for continual reassessment of the pesticide. If EPA determines at any time, that additional data are required to maintain in effect an existing registration, the Agency will require submission of such data under section 3 (c)(2)(B) of FIFRA.

2. Add the phrase EPA Registration Number "EPA Reg. No. 82076-1".

Signature of Approving Official:

Velma Noble
Regulatory Management Branch 1
Antimicrobial Division (7510C)

Date: DEC 22 2005

EPA Form 8570-6

CONCURRENCES								
SYMBOL	7510C							
SURNAME	[signature]							
DATE	12/22/05							

EPA Form 1320-1A (1/90) *Printed on Recycled Paper* **OFFICIAL FILE COPY**

3. Make the following revisions to the label.

A. Revise page the "Precautionary Statements" at the beginning of page two to read exactly as follows:

"**PRECAUTIONARY STATEMENTS**
HAZARDS TO HUMANS

DANGER Causes irreversible eye *damage*. Harmful if swallowed *or absorbed through the skin*. Do not get in eyes or on clothing. *Avoid contact with skin*. Wear safety glasses..."

B. Revise the "Direction for Use" to include the following language:

"MICROL Preservative should be added to the mineral oil...and odors in the lubricant caused by microorganisms. *Add* MICROL Preservative *at any convenient* time during the mixing process."

"*No* finished products containing MICROL Preservative may make *any* public health claims relating to antimicrobial activity without EPA pesticide registration. When incorporated into *lubricant*, this product does not protect users..."

If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA sec. 6(e). Your release for shipment of the product constitutes acceptance of these conditions.

A stamped copy of the label is enclosed for your records. Submit one (1) copy of the final printed label prior to the release of the product for shipment. If you have any questions concerning this letter, please contact Tracy Lantz at (703) 308-6415.

Sincerely,

Velma Noble
Product Manager 31
Regulatory Management Branch 1
Antimicrobial Division (7510C)

Enclosure: stamped label
7510C:T.Lantz:12/16/05:82076-1

CONCURRENCES							
SYMBOL							
SURNAME							
DATE							

MICROL* Preservative
An Antimicrobial Preservative for Industrial Use in Food Grade Lubricating Oils

KEEP OUT OF REACH OF CHILDREN

DANGER

Active ingredient
Benzoic acid 99.93%
Other ingredients (water)..... 0.07%
Total 100.00%

FIRST AID: Have the product container or label with you when calling a poison control center or doctor, or going for treatment.	
IF IN EYES	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye • Call a poison control center or doctor for treatment advice
IF INHALED	• Move person to fresh air • If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably by mouth, if possible • Call a poison control center or doctor for further treatment advice
IF SWALLOWED	• Immediately call a poison control center or doctor • Do not induct vomiting unless told to do so by a poison control center or doctor • Do not give any liquid to the person. • Do not give anything by mouth to an unconscious person
IF ON SKIN OR CLOTHING	• Take off contaminated clothing • Rinse skin immediately with plenty of water for 15-20 minutes • Call a poison control center or doctor for treatment advice
FOR 24-HOUR EMERGENCY MEDICAL ASSISTANCE, CALL THE NATIONAL POISON CONTROL CENTER 1-800-222-1222	

EPA Reg. No. xxxx-x
EPA Establishment No. xxxxx-xx-x

Net Contents: 100 lb (45.4 kg)

Petro-Canada Lubricants Division
385 Southdown Rd.
Mississauga, Ontario L5J 2Y3 CANADA

ACCEPTED
with COMMENTS
EPA Letter Dated:

[illegible] 22 [illegible]

Under the Federal Insecticide, Fungicide, and Rodenticide Act as amended, for the pesticide, registered under EPA Reg. No.

82076-1

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS

[redacted]: Causes irreversible eye injury. Harmful if swallowed. Avoid contact with skin. Do not get in eyes or on clothing. Wear safety glasses or goggles and protective gloves made of butyl rubber, PVC, or neoprene. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum or using tobacco. Remove contaminated clothing and wash before reuse.

ENVIRONMENTAL HAZARDS

Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

DIRECTIONS FOR USE

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling.

MICROL Preservative should be added to the mineral oil component of lubricants compliant with 21 CFR 178.3570 at a maximum level of 1.0%, in order to prevent decomposition and odors in the lubricant caused by microorganisms. MICROL Preservative [redacted] at any convenient time during the mixing process.

Finished products containing MICROL Preservative may [redacted] make public health claims relating to antimicrobial activity without EPA pesticide registration. When incorporated into [redacted], this product does not protect users of any such treated article or others against foodborne or disease causing bacteria, viruses, germs or other disease causing organisms.

This product is compliant with 21 CFR 184.1021.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage and disposal.

Pesticide Storage: Keep product dry during storage.

Pesticide Disposal: Wastes resulting from the use of this product must be disposed of on site or at an approved waste disposal facility.

Container Disposal: Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into application equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by state and local authorities. If drum is contaminated and cannot be reused, dispose of it in the manner required for its liner.

* MICROL is a trademark of Petro Canada

12/1/2004 Draft

ACCEPTED
with COMMENTS
EPA Letter Dated:

DEC 22 2005

Under the Federal Insecticide, Fungicide, and Rodenticide Act as amended, for the pesticide, registered under EPA Reg. No.

82076-1

Fax

To: Connie Welch

703 492 0668

From: Tracy Lantz

AD

Phone: 703 308 6415

12/22/05 1:05 PM 5 pages

Subject: Benzoic Acid

****
*** TX REPORT ***
****

TRANSMISSION OK

TX/RX NO	3609
CONNECTION TEL	917034920668
SUBADDRESS	
CONNECTION ID	
ST. TIME	12/22 14:08
USAGE T	01'58
PGS.	5
RESULT	OK

Fax

To: Connie Welch

703 492 0668

From: Tracy Lantz

AD.

Phone: 703 308 6415

12/22/05 1:05 PM 5 pages

ROUTING AND TRANSMITTAL SLIP

Date: 12/14/2005

TO: *(Name, office symbol, room number, building, Agency/Post)*	Initials	Date
1. Frank Sanders (7510C)		12/14/05
2. James Jones (7501C)		12/20
3.		
4.		
5.		
6.		
7.		
8.		
9.		
10.		

	Action		File		Note and Return
	Approval		For Clearance		Per Conversation
	As Requested		For Correction		Prepare Reply
	Circulate		For Your Information		See Me
	Comment		Investigate	X	Signature
	Coordination		Justify		Other

FROM: *(Name, org. symbol, Agency/Post)*

Environmental Protection Agency

Room No. - Bldg.

Phone No.

DO NOT use this form as a RECORD of approvals, concurrences, disposals, clearances, and similar actions.

Remarks:

OF 41 (Rev. 7-76) (E*Forms 4.4)
Prescribed by GSA
FPMR (41 CFR) 101-11.206

DEC 14 2005

6825

DEC 4 [illegible]

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

DEC

DECISION MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Registration of Benzoic Acid

FROM: Frank T. Sanders, Director
Antimicrobials Division (7510C)

TO: James Jones, Director
Office of Pesticide Programs (7501C)

REGISTRANT: Petro-Canada Specialty Products and Fluids

CHEMICAL: Benzoic Acid

PRODUCTS: MICROL Preservative (EPA File Symbol 82076-R)

Uses: Antimicrobial Preservative for Food Grade Lubricating Oils

Type of Registration: Unconditional

Missing Data: None

HIGHLIGHTS OF SCIENCE REVIEWS:

TOXICOLOGY:

Benzoic Acid is the chemical benzenecarboxylic acid ($C_7H_6O_2$) occurring in nature in free and combined forms. Toxicological data on sodium benzoate may be used to support benzoic acid since sodium benzoate is rapidly metabolized to benzoic acid in mammals. As part of its tolerance reassessment, HED has completed a review of sodium benzoate which concluded that there were no tox end points and that it may be characterized as low risk. The Food and Drug Administration has approved benzoic acid as a Generally Recognized As Safe substance (GRAS) as a direct food additive substance at 0.1% in food (21 CFR 184.1021 (d)). This ingredient is also defined as an antimicrobial agent in

21 CFR 170.3 (o)(2) and as a flavoring agent and adjuvant as defined in 170.3(o)(12). In addition, according to 40 CFR 180.910 benzoic acid is classified as an inert ingredient to be used in pre- and post-harvest with an exemption from the requirement of a tolerance as a preservative. It is ingested every day as a naturally occurring component in foods such as cranberries, prunes, plums, cinnamon, ripe cloves, while most berries contain about 0.05 percent. Benzoic acid has been used for decades in pharmaceuticals, as a pH adjustor and/or preservative in cosmetics, bath and beauty products, and as a preservative/antimicrobial agent in foods and beverages. Benzoic acid is rapidly absorbed by mammals, conjugated with glycine, and rapidly excreted in the urine as hippuric acid.

ENVIRONMENTAL FATE AND ECOLOGICAL EFFECTS:

The available ecotoxicity data for benzoic acid indicates that this compound is expected to be readily biodegradable in the environment, is of low toxicity to fish and other aquatic organisms, mammals and birds. EPA believes that benzoic acid will not cause unreasonable adverse effects on the environment. Thus no adverse impact to the environment or wildlife from exposure to benzoic acid lubricating oil products is expected. The amount of benzoic acid used in food grade lubricating oil formulations is expected to be minuscule in comparison to the amount naturally present in the environment, and is not anticipated to cause adverse effects on fish, invertebrates, plants or wildlife.

ENDANGERED SPECIES:

The use of benzoic acid as a preservative for lubricating oils is not anticipated to adversely affect endangered species due to the low toxicity of this naturally occurring compound. The amount of benzoic acid used in the registered product will result in environmental exposures which are lower than is the amount of benzoic acid naturally found in the environment, and are therefore not expected to result in any adverse effects on endangered species.

RECOMMENDATION:

I recommend that you concur with the registration of this new chemical antimicrobial under Section 3(c)(5) of the Act.

Concur Date 12/20/05

Do Not Concur Date

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DEC 20 2005

DECISION MEMORANDUM

SUBJECT: Registration of Benzoic Acid

FROM: Frank T. Sanders, Director
Antimicrobials Division (7510C)

TO: James Jones, Director
Office of Pesticide Programs (7501C)

REGISTRANT: Petro-Canada Specialty Products and Fluids

CHEMICAL: Benzoic Acid

PRODUCTS: MICROL Preservative (EPA File Symbol 82076-R)

Uses: Antimicrobial Preservative for Food Grade Lubricating Oils

Type of Registration: Unconditional

Missing Data: None

HIGHLIGHTS OF SCIENCE REVIEWS:

TOXICOLOGY:

Benzoic Acid is the chemical benzenecarboxylic acid ($C_7H_6O_2$) occurring in nature in free and combined forms. Toxicological data on sodium benzoate may be used to support benzoic acid since sodium benzoate is rapidly metabolized to benzoic acid in mammals. As part of its tolerance reassessment, HED has completed a review of sodium benzoate which concluded that there were no tox end points and that it may be characterized as low risk. The Food and Drug Administration has approved benzoic acid as a Generally Recognized As Safe substance (GRAS) as a direct food additive substance at 0.1% in food (21 CFR 184.1021 (d)). This ingredient is also defined as an antimicrobial agent in

CONCURRENCES								
SYMBOL	7510C	7510C	7510C	7510C				
SURNAME	[illegible]	V-Noble	Edwards	[illegible]				
DATE	12/13/05	12/14/05	12/14/05	12/15/05				

EPA Form 1320-1A (1/90)   Printed on Recycled Paper   OFFICIAL FILE COPY

*U.S. Government Printing Office: 1992 — [illegible]

21 CFR 170.3 (o)(2) and as a flavoring agent and adjuvant as defined in 170.3(o)(12). In addition, according to 40 CFR 180.910 benzoic acid is classified as an inert ingredient to be used in pre- and post-harvest with an exemption from the requirement of a tolerance as a preservative. It is ingested every day as a naturally occurring component in foods such as cranberries, prunes, plums, cinnamon, ripe cloves, while most berries contain about 0.05 percent. Benzoic acid has been used for decades in pharmaceuticals, as a pH adjustor and/or preservative in cosmetics, bath and beauty products, and as a preservative/antimicrobial agent in foods and beverages. Benzoic acid is rapidly absorbed by mammals, conjugated with glycine, and rapidly excreted in the urine as hippuric acid.

ENVIRONMENTAL FATE AND ECOLOGICAL EFFECTS:

The available ecotoxicity data for benzoic acid indicates that this compound is expected to be readily biodegradable in the environment, is of low toxicity to fish and other aquatic organisms, mammals and birds. EPA believes that benzoic acid will not cause unreasonable adverse effects on the environment. Thus no adverse impact to the environment or wildlife from exposure to benzoic acid lubricating oil products is expected. The amount of benzoic acid used in food grade lubricating oil formulations is expected to be minuscule in comparison to the amount naturally present in the environment, and is not anticipated to cause adverse effects on fish, invertebrates, plants or wildlife.

ENDANGERED SPECIES:

The use of benzoic acid as a preservative for lubricating oils is not anticipated to adversely affect endangered species due to the low toxicity of this naturally occurring compound. The amount of benzoic acid used in the registered product will result in environmental exposures which are lower than is the amount of benzoic acid naturally found in the environment, and are therefore not expected to result in any adverse effects on endangered species.

RECOMMENDATION:

I recommend that you concur with the registration of this new chemical antimicrobial under Section 3(c)(5) of the Act.

Concur Date

Do Not Concur Date

CONCURRENCES								
SYMBOL								
SURNAME								
DATE								

Excellent. This is fine by me
Betty

12/7/05

Betty,

Please comment,

Tracy

DECISION MEMORANDUM

SUBJECT: Registration of Benzoic Acid

FROM: Frank T. Sanders, Director
Antimicrobials Division (7510C)

TO: James Jones, Director
Office of Pesticide Programs (7501C)

REGISTRANT: Petro-Canada Specialty Products and Fluids

CHEMICAL: Benzoic Acid

PRODUCTS: MICROL Preservative (EPA File Symbol 82076-R)

Uses: Antimicrobial Preservative for Food Grade Lubricating Oils

Type of Registration: Unconditional

Missing Data: None

HIGHLIGHTS OF SCIENCE REVIEWS:

TOXICOLOGY:

Benzoic Acid is the chemical benzenecarboxylic acid ($C_7H_6O_2$) occurring in nature in free and combined forms. Toxicological data on sodium benzoate may be used to support benzoic acid since sodium benzoate is rapidly metabolized to benzoic acid in mammals. HED has completed ~~two~~ reviews on sodium benzoate which concluded that there were no tox end points and that it may be characterized as low risk. The Food and Drug

I'm not sure what this sentence means... complete 2 reviews of a complete or largely complete tox database & if so why do it twice.

Administration has approved benzoic acid as a Generally Recognized As Safe substance (GRAS) as a direct food additive substance at 0.1% in food (21 CFR 184.1021 (d)). This ingredient is also defined as an antimicrobial agent in 21 CFR 170.3 (o)(2) and as a flavoring agent and adjuvant as defined in 170.3(o)(12). In addition, according to 40 CFR 180.910 benzoic acid is classified as an inert ingredient to be used in pre- and post-harvest with an exemption from the requirement of a tolerance as a preservative. It is ingested every day as a naturally occurring component in foods such as cranberries, prunes, plums, cinnamon, ripe cloves, ~~and~~ most berries containing about 0.05 percent. Benzoic acid has been used for decades in pharmaceuticals, as a pH adjustor and/or preservative in cosmetics, bath and beauty products, and as a preservative/antimicrobial agent in foods and beverages. Benzoic acid is rapidly absorbed by mammals, conjugated with glycine, and rapidly excreted in the urine as hippuric acid.

ENVIRONMENTAL FATE AND ECOLOGICAL EFFECTS:

The available ecotoxicity data for benzoic acid indicates that this compound is expected to be readily biodegradable in the environment, is of low toxicity to fish and other aquatic organisms, mammals and birds. EPA believes that benzoic acid will not cause unreasonable adverse effects on the environment. Thus no adverse impact to the environment or wildlife from exposure to benzoic acid lubricating oil products is expected. The amount of benzoic acid used in lubricating oil formulations is expected to be minuscule in comparison to the amount naturally present in the environment, and is not anticipated to cause adverse effects on fish, invertebrates, plants or wildlife.

ENDANGERED SPECIES:

The use of benzoic acid as a preservative for lubricating oils is not anticipated to adversely affect endangered species due to the low toxicity of this naturally occurring compound. The amount of benzoic acid used in the registered product will result in environmental exposures which are lower than the amount of benzoic acid naturally found in the environment, and are therefore not expected to result in any adverse effects on endangered species.

RECOMMENDATION:

I recommend that you concur with the registration of this new chemical antimicrobial under Section 3(c)(5) of the Act.

_____

Concur Date

_____

Do Not Concur Date

Category of food	Maximum level of use in food (as served)	Functional use
Soup and soup mixes, § 170.3(n) (40) of this chapter.	Not to exceed current good manufacturing practice.	Emulsifier, emulsifier salt, § 170.3(o)(8) of this chapter; texturizer, acid, § 170.3(o)(14) of this chapter; stabilizer, thickener, § 170.3(o)(28) of this chapter

(d) Prior sanctions for this ingredient different from the use established in this section do not exist or have been waived.

[47 FR 47375, Oct. 26, 1982]

§ 184.1012 α-Amylase enzyme preparation from Bacillus stearothermophilus.

(a) α-Amylase enzyme preparation is obtained from the culture filtrate that results from a pure culture fermentation of a nonpathogenic and nontoxicogenic strain of *Bacillus stearothermophilus*. Its characterizing enzyme activity is α-amylase (1,4 α-D-glucan glucanohydrolase (E.C. 3.2.1.1)).

(b) The ingredient meets the general and additional requirements for enzyme preparations in the "Food Chemicals Codex," 3d ed. (1981), pp. 107–110, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of Premarket Approval (HFS–200), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 1110 Vermont Ave. NW., suite 1200, Washington, DC, or the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with §184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practices. The affirmation of this ingredient as GRAS as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme, as defined in §170.3(o)(9) of this chapter, in the hydrolysis of edible starch to produce maltodextrins and nutritive carbohydrate sweeteners.

(2) The ingredient is used at levels not to exceed current good manufacturing practices.

[60 FR 55799, Nov. 3, 1995]

§ 184.1021 Benzoic acid.

(a) Benzoic acid is the chemical benzenecarboxylic acid ($C_7H_6O_2$), occurring in nature in free and combined forms. Among the foods in which benzoic acid occurs naturally are cranberries, prunes, plums, cinnamon, ripe dates, and most berries. Benzoic acid is manufactured by treating molten phthalic anhydride with steam in the presence of a zinc oxide catalyst, by the hydrolysis of benzotrichloride, or by the oxidation of toluene with nitric acid or sodium bichromate or with air in the presence of a transition metal salt catalyst.

(b) The ingredient meets the specifications of the "Food Chemicals Codex," 3d Ed. (1981), p. 35, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as an antimicrobial agent as defined in §170.3(o)(2) of this chapter, and as a flavoring agent and adjuvant as defined in §170.3(o)(12) of this chapter.

(d) The ingredient is used in food at levels not to exceed good manufacturing practice. Current usage results in a maximum level of 0.1 percent in food. (The Food and Drug Administration has not determined whether significantly different conditions of use would be GRAS).

(e) Prior sanctions for this ingredient different from those uses established in this section, or different from that set forth in part 181 of this chapter, do not exist or have been waived.

[42 FR 14653, Mar. 15, 1977, as amended at 49 FR 5610, Feb. 14, 1984]

§ 184.1024 Bromelain.

(a) Bromelain (CAS Reg. No. 9001–00–7) is an enzyme preparation derived from the pineapples *Ananas comosus* and *A. bracteatus* L. It is a white to light tan amorphous powder. Its characterizing enzyme activity is that of a peptide hydrolase (EC 3.4.22.32).

(b) The ingredient meets the general requirements and additional requirements for enzyme preparations in the Food Chemicals Codex, 3d ed. (1981), p. 110, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC, or may be examined at the Office of Premarket Approval (HFS–200), Food and Drug Administration, 200 C St. SW., Washington, DC, and the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with §184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as GRAS as a direct food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme as defined in §170.3(o)(9) of this chapter to hydrolyze proteins or polypeptides.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

[60 FR 32910, June 26, 1995]

§ 184.1025 Caprylic acid.

(a) Caprylic acid [$CH_3(CH_2)_6COOH$, CAS Reg. No. 124–07–2] is the chemical name for octanoic acid. It is considered to be a short or medium chain fatty acid. It occurs normally in various foods and is commercially prepared by oxidation of n-octanol or by fermentation and fractional distillation of the volatile fatty acids present in coconut oil.

(b) The ingredient meets the specifications of the "Food Chemicals Codex," 3d Ed. (1981), p. 207, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW.,

incorporate into menu
need slightly

PESTICIDE FACT SHEET

Name of Chemical: Benzenecarboxylic Acid ($C_7H_6O_2$)
Reason of Issuance: New Chemical Registration
Date Issued:
Fact Sheet Number:

Description of Chemical

Chemical Name: Benzenecarboxylic Acid ($C_7H_6O_2$)

Common Name: Benzoic Acid

Product Trade Name: MICROL Preservative

Chemical Abstract Number (CAS): 65-85-0

EPA Chemical Code: 009101

Chemical Family: Carboxylic Acid

Year of Initial Registration: 2005

Pesticide Type: Preservative for Food-Grade Lubricating Oils

U.S. Producer: Petro Canada
Specialty Products and Fluids
2489 North Sheridan Way
Mississauga, Ontario L5K 1A8 CANADA

Use Patterns and Formulation

Pesticide Type: End Use Product for use as a Preservative for Food-Grade Lubricating Oils

Science Findings

Summary Science Statement

The submitted product chemistry data, for Benzoic acid satisfies product chemistry OPPTS Guideline Series 830. Toxicological data on sodium benzoate may be used to support benzoic acid since sodium benzoate is rapidly metabolized to benzoic acid in mammals. As part of its tolerance reassessment, HED has completed a review of sodium benzoate which concluded that there were no tox end points and that it may be characterized as low risk. The Food and Drug Administration has approved benzoic acid as a Generally Recognized As Safe substance (GRAS) as a direct food additive substance at 0.1% in food (21 CFR 184.1021 (d)). This ingredient is also defined as an antimicrobial agent in 21 CFR 170.3 (o)(2) and as a flavoring agent and adjuvant as defined in 170.3(o)(12). In addition, according to 40 CFR 180.910 benzoic acid is classified as an inert ingredient to be used in pre- and post-harvest with an exemption from the requirement of a tolerance as a preservative. It is ingested every day as a naturally occurring component in foods such as cranberries, prunes, plums, cinnamon, ripe cloves, while most berries contain about 0.05 percent. Benzoic acid has been used for decades in pharmaceuticals, as a pH adjustor and/or preservative in cosmetics, bath and beauty products, and as a preservative/antimicrobial agent in foods and beverages. Benzoic acid is rapidly absorbed by mammals, conjugated with glycine, and rapidly excreted in the urine as hippuric acid.

The available ecotoxicity data for benzoic acid indicates that this compound is expected to be readily biodegradable in the environment, is of low toxicity to fish and other aquatic organisms, mammals and birds. EPA believes that benzoic acid will not cause unreasonable adverse effects on the environment. Thus no adverse impact to the environment or wildlife from exposure to benzoic acid lubricating oil products is expected. The amount of benzoic acid used in food grade lubricating oil formulations is expected to be minuscule in comparison to the amount naturally present in the environment, and is not anticipated to cause adverse effects on fish, invertebrates, plants or wildlife.

Physical and Chemical Characteristics

Color:	White
Physical State:	Solid (crystalline powder)
Melting Point	122 °C
Specific Gravity	1.2659
Odor:	Odorless-to-slight benzaldehyde

Water Partition Coefficient:	log Kow is 1.87
pH:	2.8
Stability:	Stable
Oxidizing or Reducing Action:	Contains no oxidizing/reducing agents. May react with oxidizers.
Flammability:	Not Applicable, Flash point 250°F by closed cup.
Explodability:	Does not contain any explodable components
Viscosity:	Not Applicable
Corrosion Characteristics:	Does not react with packaging

Toxicology Profile

Technical Acute Toxicity	Status	Toxicity Category
Acute Oral	Fulfilled	III
Acute Dermal	Fulfilled	III
Acute Inhalation	Fulfilled	IV
Primary Eye Irritation	Fulfilled	I
Primary Skin Irritation	Fulfilled	III
Dermal Sensitization	Fulfilled	Non-Sensitizing

The Agency did not require subchronic/chronic studies for benzoic acid because it occurs in nature in free and combined forms. FDA has approved benzoic acid as a GRAS substance that can be added directly to food at 0.1% or less. Benzoic acid is a naturally occurring component in foods such as cranberries, prunes, plums, cinnamon and cloves. Most berries contain approximately 0.05% benzoic acid.

Environmental Fate and Ecological Effect

The Agency did not require ecological effect or environmental fate data for benzoic acid because it occurs in nature in free and combined forms and is expected to readily biodegrade.

Contact Person at EPA

Velma Noble
Product Manager (31)
Regulatory Management Branch 1
Antimicrobials Divison (7510C)
Office of Pesticide Programs
(703) 308-6233

Mailing Address:

By US Mail

Document Processing Desk
Office of Pesticide Programs (7510C)
US Environmental Protection Agency
1200 Pennsylvania Ave, NW
Washington, DC 20460-0001

By Courier:

Document Processing Desk
Office of Pesticide Programs (7510C)
US Environmental Protection Agency
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

Office Location and Telephone Number - Antimicrobials Division

Third Floor, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202
(703) 308-6411

Disclaimer: The information in this Pesticide Fact Sheet is a summary only and is not to be used to satisfy any data requirements for pesticide registration or reregistration.

Product ingredient source information may be entitled to confidential treatment

PESTICIDE FACT SHEET

12/13/05 copy to Dennis for review

Name of Chemical: Benzenecarboxylic Acid ($C_7H_6O_2$)
Reason of Issuance: New Chemical Registration
Date Issued:
Fact Sheet Number:

Description of Chemical

Chemical Name: Benzenecarboxylic Acid ($C_7H_6O_2$)

Common Name: Benzoic Acid

Product Trade Name: MICROL Preservative

Chemical Abstract Number (CAS): 65-85-0

EPA Chemical Code: ***Ask Bob Turpin-can't read*** – 009101 check w/ maj im. sent him a note on 12/16

Chemical Family: ***don't know*** (carboxylic acids)

Year of Initial Registration: ***don't know*** 2005

Pesticide Type: Preservative for Food-Grade Lubricating Oils

U.S. Producer: [redacted] Petro Canada

Use Patterns and Formulation

Pesticide Type: End Use Product for use as a Preservative for Food-Grade Lubricating Oils

Science Findings

Summary Science Statement

The submitted product chemistry data, for Benzoic acid satisfies product chemistry OPPTS Guideline Series 830. Toxicological data on sodium benzoate may be used to support benzoic acid since sodium benzoate is rapidly metabolized to benzoic acid in mammals. As part of its tolerance reassessment, HED has completed a review of sodium benzoate which concluded that there were no tox end points and that it may be characterized as low risk. The Food and

Drug Administration has approved benzoic acid as a Generally Recognized As Safe substance (GRAS) as a direct food additive substance at 0.1% in food (21 CFR 184.1021 (d)). This ingredient is also defined as an antimicrobial agent in 21 CFR 170.3 (o)(2) and as a flavoring agent and adjuvant as defined in 170.3(o)(12). In addition, according to 40 CFR 180.910 benzoic acid is classified as an inert ingredient to be used in pre- and post-harvest with an exemption from the requirement of a tolerance as a preservative. It is ingested every day as a naturally occurring component in foods such as cranberries, prunes, plums, cinnamon, ripe cloves, while most berries contain about 0.05 percent. Benzoic acid has been used for decades in pharmaceuticals, as a pH adjustor and/or preservative in cosmetics, bath and beauty products, and as a preservative/antimicrobial agent in foods and beverages. Benzoic acid is rapidly absorbed by mammals, conjugated with glycine, and rapidly excreted in the urine as hippuric acid.

The available ecotoxicity data for benzoic acid indicates that this compound is expected to be readily biodegradable in the environment, is of low toxicity to fish and other aquatic organisms, mammals and birds. EPA believes that benzoic acid will not cause unreasonable adverse effects on the environment. Thus no adverse impact to the environment or wildlife from exposure to benzoic acid lubricating oil products is expected. The amount of benzoic acid used in food grade lubricating oil formulations is expected to be minuscule in comparison to the amount naturally present in the environment, and is not anticipated to cause adverse effects on fish, invertebrates, plants or wildlife.

Physical and Chemical Characteristics

Color:	White
Physical State:	Solid (crystalline powder)
Melting Point	122 °C
Specific Gravity	1.2659
Odor:	Odorless-to-slight benzaldehyde
Water Partition Coefficient:	log Kow is 1.87
pH:	2.8
Stability:	Stable
Oxidizing or Reducing Action:	Contains no oxidizing/reducing agents. May react with oxidizers.

Flammability:	Not Applicable, Flash point 250°F by closed cup.
Explodability:	Does not contain any explodable components
Viscosity:	Not Applicable
delete ~~Miscibility:~~	~~Not Applicable, if product is an emulsifiable liquid~~
Corrosion Characteristics:	Does not react with packaging
delete ~~Dielectric Breakdown Voltage:~~	~~Not applicable~~

Toxicology Profile

Technical Acute Toxicity	Status	Toxicity Category
Acute Oral	Fulfilled	III
Acute Dermal	Fulfilled	III
Acute Inhalation	Fulfilled	IV
Primary Eye Irritation	Fulfilled	I
Primary Skin Irritation	Fulfilled	III
Dermal Sensitization	Fulfilled	Non-Sensitizing
Short Term/Subchronic Toxicity	?	
Developmental/Reproductive Toxicity	?	
Carcinogenicity	?	
Mutagenicity	?	

The Agency did not require subchronic/chronic studies for benzoic acid because it occurs in nature in free and combined forms. FDA has approved benzoic acid as a GRAS substance that can be added directly to food at 0.1% or less. Benzoic acid is a naturally occurring component in foods such as cranberries, prunes, plums, cinnamon and cloves. Most berries contain approximately 0.05% benzoic acid.

Environmental Fate and Ecological Effect

(Don't know what I should do in this section)

~~Ecological Effects~~ ~~**~~Waiver

The Agency did not require ecological effects or environmental fate data for benzoic acid because it occurs in nature in free and combined forms and is expected to readily biodegrade.

Environmental Fate ..... **Waiver

* Subchronic, chronic and mutagenicity and exposure data requirements are all waived for calcium carbonate. This chemical is a naturally occurring substance, one of the mot common compounds on earth and is ingested daily with no apparent harm.

** All environmental fate and ecological effects data were waived for this chemical due to the fact that it is an integral part of environment and ecological systems. No adverse impact to the environment or wildlife from exposure to calcium carbonate based paint products is expected since the amount of calcium carbonate used in paint formulations is expected to be minuscule in comparison to the amount naturally present in the environment, and thus would not significantly effect the environment or wildlife.

Contact Person at EPA

Velma Noble
Product Manager (31)
Regulatory Management Branch 1
Antimcrobials Divison (7510C)
Office of Pesticide Programs
(703) 308-6233

Mailing Address:

By US Mail

Document Processing Desk
Office of Pesticide Programs (7510C)
US Environmental Protection Agency
1200 Pennsylvania Ave, NW
Washington, DC 20460-0001

By Courier:

Document Processing Desk\
Office of Pesticide Programs (7510C)
US Environmental Protection Agency
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

Office Location and Telephone Number - Antimicrobials Division

Third Floor, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202
(703) 308-6411

Disclaimer: The information in this Pesticide Fact Sheet is a summary only and is not to be used to satisfy any data requirements for pesticide registration or reregistration.

Product ingredient source information may be entitled to confidential treatment

PESTICIDE FACT SHEET

12/13/05

Dennis,

Please review + comment.

Tracy

Name of Chemical: Benzenecarboxylic Acid ($C_7H_6O_2$)
Reason of Issuance: New Chemical Registration
Date Issued:
Fact Sheet Number:

Description of Chemical

Chemical Name: Benzenecarboxylic Acid ($C_7H_6O_2$)

Common Name: Benzoic Acid

Product Trade Name: MICROL Preservative

Chemical Abstract Number (CAS): 65-85-0

EPA Chemical Code: ***Ask Bob Turpin-can't read***

Chemical Family: ***don't know***

Year of Initial Registration: ***don't know***

Pesticide Type: Preservative for Food-Grade Lubricating Oils

U.S. Producer: [redacted]

Use Patterns and Formulation

Pesticide Type: End Use Product for use as a Preservative for Food-Grade Lubricating Oils

Science Findings

Summary Science Statement

The submitted product chemistry data, for Benzoic acid satisfies product chemistry OPPTS Guideline Series 830. Toxicological data on sodium benzoate may be used to support benzoic acid since sodium benzoate is rapidly metabolized to benzoic acid in mammals. As part of its tolerance reassessment, HED has completed a review of sodium benzoate which concluded that there were no tox end points and that it may be characterized as low risk. The Food and

Drug Administration has approved benzoic acid as a Generally Recognized As Safe substance (GRAS) as a direct food additive substance at 0.1% in food (21 CFR 184.1021 (d)). This ingredient is also defined as an antimicrobial agent in 21 CFR 170.3 (o)(2) and as a flavoring agent and adjuvant as defined in 170.3(o)(12). In addition, according to 40 CFR 180.910 benzoic acid is classified as an inert ingredient to be used in pre- and post-harvest with an exemption from the requirement of a tolerance as a preservative. It is ingested every day as a naturally occurring component in foods such as cranberries, prunes, plums, cinnamon, ripe cloves, while most berries contain about 0.05 percent. Benzoic acid has been used for decades in pharmaceuticals, as a pH adjustor and/or preservative in cosmetics, bath and beauty products, and as a preservative/antimicrobial agent in foods and beverages. Benzoic acid is rapidly absorbed by mammals, conjugated with glycine, and rapidly excreted in the urine as hippuric acid.

The available ecotoxicity data for benzoic acid indicates that this compound is expected to be readily biodegradable in the environment, is of low toxicity to fish and other aquatic organisms, mammals and birds. EPA believes that benzoic acid will not cause unreasonable adverse effects on the environment. Thus no adverse impact to the environment or wildlife from exposure to benzoic acid lubricating oil products is expected. The amount of benzoic acid used in food grade lubricating oil formulations is expected to be minuscule in comparison to the amount naturally present in the environment, and is not anticipated to cause adverse effects on fish, invertebrates, plants or wildlife.

Physical and Chemical Characteristics

Color:	White
Physical State:	Solid (crystalline powder)
Melting Point	122 °C
Specific Gravity	1.2659
Odor:	Odorless-to-slight benzaldehyde
Water Partition Coefficient:	log Kow is 1.87
pH:	2.8
Stability:	Stable
Oxidizing or Reducing Action:	Contains no oxidizing/reducing agents. May react with oxidizers.

Flammability:	Not Applicable, Flash point 250°F by closed cup.
Explodability:	Does not contain any explodable components
Viscosity:	Not Applicable
Miscibility:	Not Applicable, if product is an emulsifiable liquid
Corrosion Characteristics:	Does not react with packaging
Dielectric Breakdown Voltage:	Not applicable

Toxicology Profile

Technical Acute Toxicity	Status	Toxicity Category
Acute Oral	Fulfilled	III
Acute Dermal	Fulfilled	III
Acute Inhalation	Fulfilled	IV
Primacy Eye Irritation	Fulfilled	I
Primary Skin Irritation	Fulfilled	III
Dermal Sensitization	Fulfilled	Non-Sensitizing
Short Term/Subchronic Toxicity	?	
Developmental/Reproductive Toxicity	?	
Carcinogenicity	?	
Mutagenicity	?	

Environmental Fate and Ecological Effect

(Don't know what I should do in this section)

Ecological Effects	**Waiver

Environmental Fate	**Waiver

* Subchronic, chronic and mutagenicity and exposure data requirements are all waived for calcium carbonate. This chemical is a naturally occurring substance, one of the mot common compounds on earth and is ingested daily with no apparent harm.
** All environmental fate and ecological effects data were waived for this chemical due to the fact that it is an integral part of environment and ecological systems. No adverse impact to the environment or wildlife from exposure to calcium carbonate based paint products is expected since the amount of calcium carbonate used in paint formulations is expected to be minuscule in comparison to the amount naturally present in the environment, and thus would not significantly effect the environment or wildlife.

Contact Person at EPA

Velma Noble
Product Manager (31)
Regulatory Management Branch I
Antimicrobials Divison (7510C)
Office of Pesticide Programs
(703) 308-6233

Mailing Address:

By US Mail

Document Processing Desk
Office of Pesticide Programs (7510C)
US Environmental Protection Agency
1200 Pennsylvania Ave, NW
Washington, DC 20460-0001

By Courier:

Document Processing Desk
Office of Pesticide Programs (7510C)
US Environmental Protection Agency
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

Office Location and Telephone Number - Antimicrobials Division

Third Floor, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202
(703) 308-6411

Disclaimer: The information in this Pesticide Fact Sheet is a summary only and is not to be used to satisfy any data requirements for pesticide registration or reregistration.

TO: RASSB 1

PRIA

TASK ASSIGNMENT FORM
Antimicrobial Division/Regulatory Management Branch II

A	Completed by Product Manager	
PRODUCT REVIEWER: Tracy		RMB II TEAM
Description of Action: Bean Sheet For Bob Quick		EPA File Symbol/Reg No. 82076-R
Decision No.	Submission No.	Fee for Service Action Code: A38
FQPA Action Code:	Non-FQPA Action Code:	Fee for Service Fee: $ 90,010

	MONTH	DAY	YEAR
APPLICATION DATE	2	9	2005
EPA PIN DATE	2	9	2005
REVIEWER ASSIGNED DATE			2005
DATE DUE FROM SCIENCE			2005
DATE DUE TO PM			2005

Type of Data:	PSB Product Chemistry ☐	PSB Acute Toxicology ☐	PSB Efficacy ☐	RASSB Environmental Fate ☐	RASSB Ecological Effects ☐	RASSB Chronic Toxicology ☐	RASSB Exposure ☐

COMMENTS: NOTE TO ARCTIC SLOPE - PLEASE COMPLETE PART B OF FORM.

To Bob Quick - Please confirm with a ~~Letter~~ level of Benzoic Acid in Food.

ATTACHMENTS: ☐-LABELING ☐-CSF(S) ☐-DATA ☐-OTHERS

B	For Arctic Slope Contract Only	
Contractor: Arctic Slope	Contract No.: 0332	ARCTIC SLOPE/MANAGER
Draft Task: Signature _____ (Est. hrs)	Final Task: Signature _____ (Total hrs)	

C Reviewer's Comments:

DATE FEE PAID: _____ RESPONSE CODE: _____ RESPONSE DATE: _____

DP #: (315791)

Decision #: 352089

DATA PACKAGE BEAN SHEET

Date: 11-Apr-2005

PRIA

* * * Registration Information * * *

Registration: 82076-R - MICROL PRESERVATIVE

Company: 82076 - PETRO-CANADA

Risk Manager: RM 31 - Velma Noble - (703) 308-8233 Room# CM-2 308B

Risk Manager Reviewer: Tracy Lantz TLANTZ

Sent Date: 09-Feb-2005 Calculated Due Date: 4/1/05 Edited Due Date:

Type of Registration: Product Registration - Section 3

Action Desc: (A38) NEW AI;FOOD USE;WITH EXEMPTION;

Ingredients: 009101, Benzoic acid(99.93%)

* * * Data Package Information * * *

Expedite: ○ Yes ● No Date Sent: 11-Apr-2005 Due Back:

DP Ingredient: 009101, Benzoic acid

DP Title:

CSF Included: ○ Yes ● No Label Included: ○ Yes ● No Parent DP #:

Assigned To	Date In	Date Out
Organization: AD / RASSB		
Team Name: RASSB1		
Reviewer Name:		
Contractor Name:		

7/1/05

Administrative Due Date:

Negotiated Due Date:

Projected Completion Date:

* * * Studies Sent for Review * * *

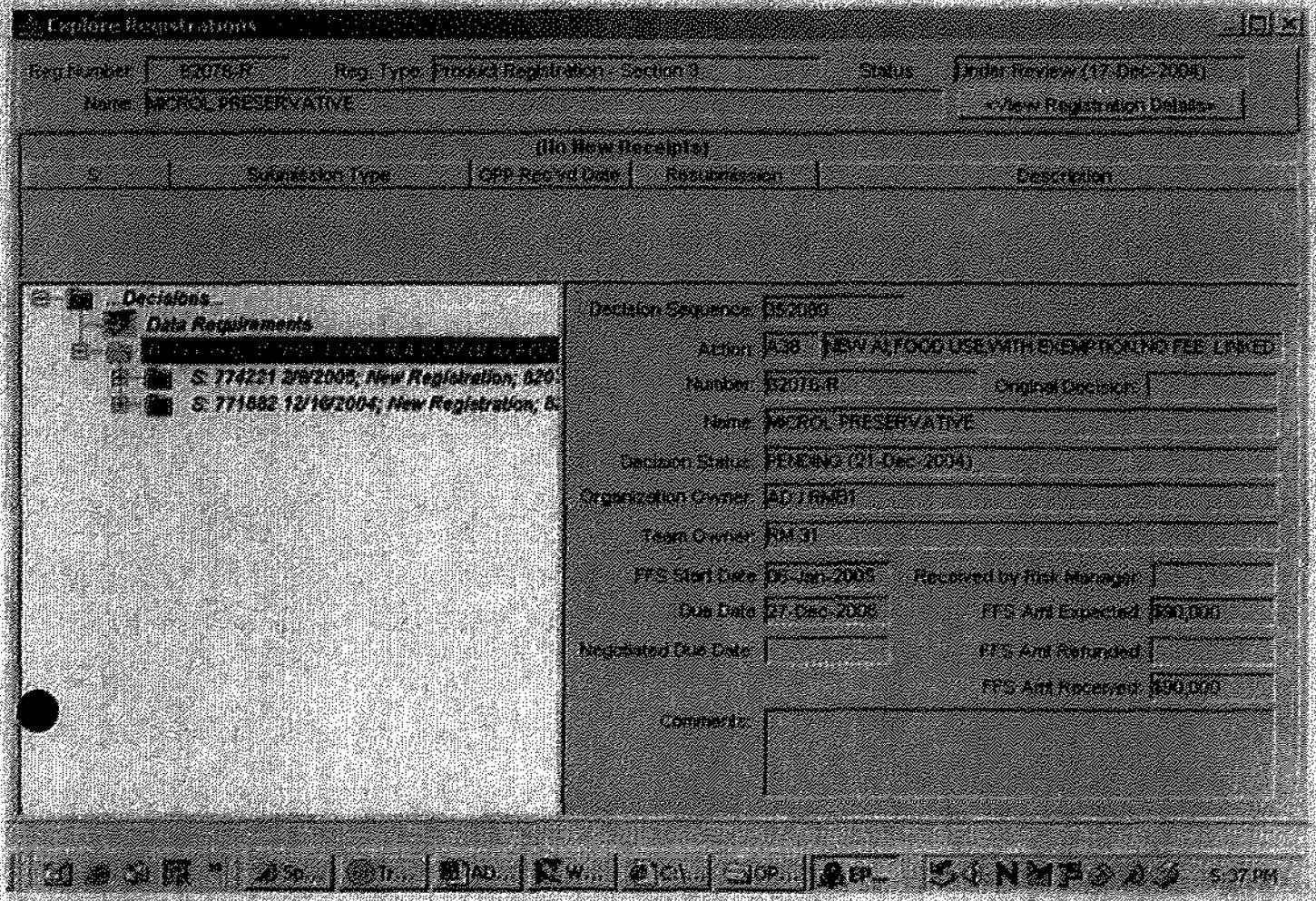
No Studies

* * * Additional Data Package for this Decision * * *

Printed on Page 2

* * * Data Package Instructions * * *

Please have Bob Quick confirm the companies PPM calculations he has the information needed to do this.


Explore Registrations
Reg Number: 62078-R
Reg Type: Revised Registration - Section 3
Status: Under Review (17-Dec-2004)
Name: MICROL PRESERVATIVE
<<New Registration Details>>
(No New Receipts)
S
Submission Type
OPP Receipt Date
Resubmission
Description
Decisions...
Data Requirements
S: 774221 2/9/2005; New Registration, 62078-R
S: 771682 12/16/2004; New Registration, 62078-R
Decision Sequence: 052.000
Action: 4.38 NEW ALT FOOD USE WITH EXEMPTION, NO FEE LANGUAGE
Number: 62078-R
Original Decision:
Name: MICROL PRESERVATIVE
Decision Status: PENDING (21-Dec-2004)
Organization Owner: AD (RMB1)
Team Owner: RM 31
FFS Start Date: 05-Jan-2005
Received by Risk Manager:
Due Date: 27-Dec-2005
FFS Amt Expected: $30,000
Negotiated Due Date:
FFS Amt Returned:
FFS Amt Received: $30,000
Comments:
5:37 PM

Wallace Powell/DC/USEPA/US
11/30/2005 10:09 AM

To Tracy Lantz/DC/USEPA/US@EPA
cc
bcc
Subject Re: tox label review for Benzoic Acid

Tracy
I'm going to work on it Monday. So I'll give the draft to Karen to sign (and email the draft to you) on Monday or Tuesday.
(I wish I could do better than that, but there's something else I need to finish this week.)

Tracy Lantz/DC/USEPA/US

Tracy Lantz/DC/USEPA/US
11/29/05 16:33

To Wallace Powell/DC/USEPA/US@EPA
cc
Subject tox label review for Benzoic Acid

How's the review coming along?
I am hoping that you can get it to me ASAP as I am ready to move forward and am now just waiting for your review.

Thanks.

Decision #: 352089

DATA PACKAGE BEAN SHEET

DP #: (315790)

Date: 02-Sep-2005

* * * Registration Information * * *

Registration: 82076-R - MICROL PRESERVATIVE

Company: 82076 - PETRO-CANADA

Risk Manager: RM 31 - Velma Noble - (703) 308-6233 Room# CM-2 308B

Risk Manager Reviewer: Tracy Lantz TLANTZ

Sent Date: Calculated Due Date: 27-Dec-2006 Edited Due Date:

Type of Registration: Product Registration - Section 3

Action Desc: (A38) NEW AI;FOOD USE;WITH EXEMPTION;

Ingredients: 009101, Benzoic acid(99.93%)

* * * Data Package Information * * *

Expedite: ○ Yes ● No Date Sent: 11-Apr-2005 Due Back:

DP Ingredient: 009101, Benzoic acid

DP Title:

CSF Included: ● Yes ○ No Label Included: ● Yes ○ No Parent DP #:

Assigned To	Date In	Date Out	
Organization: AD / PSB	13-Apr-2005		Last Possible Science Due Date: 22-May-2006
Team Name: CTT	13-Apr-2005		Science Due Date: 01-Aug-2005
Reviewer Name: Powell, Wallace	15-Apr-2005		Sub Data Package Due Date: 17-Jul-2005
Contractor Name:			

* * * Studies Sent for Review * * *

No Studies

* * * Additional Data Package for this Decision * * *

Printed on Page 2

* * * Data Package Instructions * * *

Karen Tox -- Here are the HED reviews (Risk Assessment) to do acute tox based on Sodium Benzoate.

Tracy Lantz/DC/USEPA/US
10/31/2005 04:05 PM

To Wallace Powell/DC/USEPA/US
cc
bcc
Subject Fw: acute tox for benzoic acid

I don't recall that I have received this review from you.
Do I have it and I have forgotten, or have you not yet given it to me?
Please look into this as Dennis wants me to complete this package and I need your information to do so.
Thanks,
Tracy
----- Forwarded by Tracy Lantz/DC/USEPA/US on 10/31/2005 04:08 PM -----

Wallace Powell/DC/USEPA/US
09/14/2005 02:34 PM

To Tracy Lantz/DC/USEPA/US@EPA
cc
Subject Re: acute tox for benzoic acid

Yes I will. I'll give you a draft (& submit it for signature) next week
wallace

Tracy Lantz/DC/USEPA/US

Tracy Lantz/DC/USEPA/US
09/13/05 16:30

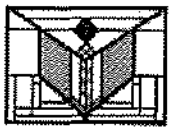
To Wallace Powell/DC/USEPA/US@EPA
cc Velma Noble/DC/USEPA/US@EPA
Subject acute tox for benzoic acid

It appears that you still have an outstanding data package for 82076-R that we gave to you back in April. The package included HED risk assessments on Sodium Benzoate. We would like you to give your opinion, based on those reviews, as to whether the precautionary statements for this product are accurate.

This is D 352089, DP 315790

This new active ingredient is due out of the Agency in the next few months, so I would like your review as soon as possible.

Thanks



Tracy Lantz/DC/USEPA/US
09/13/2005 04:18 PM

To Wallace Powell/DC/USEPA/US
cc Velma Noble/DC/USEPA/US
bcc
Subject acute tox for benzoic acid

It appears that you still have an outstanding data package for 82076-R that we gave to you back in April. The package included HED risk assessments on Sodium Benzoate. We would like you to give your opinion, based on those reviews, as to whether the precautionary statements for this product are accurate.

This is D 352089, DP 315790

This new active ingredient is due out of the Agency in the next few months, so I would like your review as soon as possible.

Thanks.

Data Package Information for D: Pending; 352089; 82076 R.A.38;NEW AI;FOOD USE WITH EXEMPTION

DP Sequence: 315790 Expedite: Yes No Label: Yes No CSF: Yes No

Bean Count: 1 Data Package Title:

Parent DP #: Data Package Type:

Instructions: Karen Tox -- Here are the HED reviews (Risk Assessment) to do acute tox based on Sodium Benzoate.

Bean Sheet

Data Package Comments | Waiver Documentation

Sent To | Sent From | DP Dates | MRIDS | Sub-DP | DP Ingredients | DP Contract | Receipts

Organization Name: AD / PSB

Date Received: 13-Apr-2005 Date Completed:

Team Name	Team Description	Date Received	Date Completed
CTT	AD/PSB Chemistry/Toxicology Team	13-Apr-2005	

1 Team(s) Linked

Staff Name	Est. Hrs.	Actual Hrs.	Date Received	Date Completed
Powell, Wallace			15-Apr-2005	

1 Staff Member(s) Linked

Viewing Record 1 of 1

9/12/05

TKAcy

It appears that Wallace still needs to do a profile on the acute toxicity of benzoic Acid. You probably need to CALL him about this and see if he can go ahead & look at it → If need be have Velma talk w/ Karen

Dennis

Please talk w/ Wallace About the status of the review

Sent attached note to Wallace on 9/13/05 + 10/31/05

DP # (315790) Decision #: 352089

DATA PACKAGE BEAN SHEET

Date: 11-Apr-2005

* * * Registration Information * * *

Registration: 82076-R - MICROL PRESERVATIVE

Company: 82076 - PETRO-CANADA

Risk Manager: RM 31 - Velma Noble - (703) 308-6233 Room# CM-2 308B

Risk Manager Reviewer: Tracy Lantz TLANTZ

Sent Date: Calculated Due Date: 9/1/05 Edited Due Date:

Type of Registration: Product Registration - Section 3

Action Desc: (A38) NEW AI:FOOD USE;WITH EXEMPTION;

Ingredients: 009101, Benzoic acid(99.93%)

* * * Data Package Information * * *

Expedite: ○ Yes ● No Date Sent: 11-Apr-2005 Due Back:

DP Ingredient: 009101, Benzoic acid

DP Title:

CSF Included: ● Yes ○ No Label Included: ● Yes ○ No Parent DP #:

Assigned To	Date In	Date Out
Organization: AD / PSB		
Team Name: CTT		
Reviewer Name:		
Contractor Name		

7/1/05

Administrative Due Date: ~~01-Apr-2007~~

Negotiated Due Date:

Projected Completion Date:

* * * Studies Sent for Review * * *

No Studies

* * * Additional Data Package for this Decision * * *

Printed on Page 2

* * * Data Package Instructions * * *

Karen Tox – Here are the HED reviews (Risk Assessment) to do acute tox based on Sodium Benzoate.

PRIA

TASK ASSIGNMENT FORM
Antimicrobial Division/Regulatory Management Branch II

A	Completed by Product Manager		
PRODUCT REVIEWER: Tray		RMB II	TEAM
Description of Action: Bean sheet for Kalen Hicks Acute Tox		EPA File Symbol/Reg No. 82076-R	
Decision No. 352089	Submission No. 774221	Fee for Service Action Code: A38	
FQPA Action Code:	Non-FQPA Action Code:	Fee for Service Fee: $ 90,000	

	MONTH	DAY	YEAR
APPLICATION DATE	2	9	2005
EPA PIN DATE	2	9	2005
REVIEWER ASSIGNED DATE			2005
DATE DUE FROM SCIENCE			2005
DATE DUE TO PM			2005

Type of Data:	PSB Product Chemistry ☐	PSB Acute Toxicology ☒	PSB Efficacy ☐	RASSB Environmental Fate ☐	RASSB Ecological Effects ☐	RASSB Chronic Toxicology ☐	RASSB Exposure ☐

COMMENTS: NOTE TO ARCTIC SLOPE - PLEASE COMPLETE PART B OF FORM.

Kalen Tox — Here are the HED reviews (Risk Assesment) to do acute tox based on Sodium Benzoate.

ATTACHMENTS: ☐-LABELING ☐-CSF(S) ☐-DATA ☐-OTHERS

B	For Arctic Slope Contract Only		
Contractor: Arctic Slope		Contract No.: 0332	ARCTIC SLOPE/MANAGER
Draft Task: Signature _____ (Est. hrs)		Final Task: Signature _____ (Total hrs)	

C Reviewer's Comments:

DATE FEE PAID:_____ RESPONSE CODE:_____ RESPONSE DATE:_____

Decision #: 352089

DATA PACKAGE BEAN SHEET

DP #: (315790)

Date: 01-Nov-2005

* * * Registration Information * * *

Registration: 82076-R - MICROL PRESERVATIVE

Company: 82076 - PETRO-CANADA

Risk Manager: RM 31 - Velma Noble - (703) 308-8233 Room# CM-2 308B

Risk Manager Reviewer: Tracy Lantz TLANTZ

Sent Date: Calculated Due Date: 27-Dec-2006 Edited Due Date:

Type of Registration: Product Registration - Section 3

Action Desc: (A38) NEW AI;FOOD USE;WITH EXEMPTION;NO FEE; LINKED TO A PRIA APPLICATION;

Ingredients: 009101, Benzoic acid(99.93%)

* * * Data Package Information * * *

Expedite: ○ Yes ● No Date Sent: 11-Apr-2005 Due Back:

DP Ingredient: 009101, Benzoic acid

DP Title:

CSF Included: ● Yes ○ No Label Included: ● Yes ○ No Parent DP #:

Assigned To	Date In	Date Out		
Organization: AD / PSB	13-Apr-2005		Last Possible Science Due Date:	22-May-2006
Team Name: CTT	13-Apr-2005		Science Due Date:	01-Aug-2005
Reviewer Name: Powell, Wallace	15-Apr-2005		Sub Data Package Due Date:	17-Jul-2005
Contractor Name:				

* * * Studies Sent for Review * * *

No Studies

* * * Additional Data Package for this Decision * * *

Printed on Page 2

* * * Data Package Instructions * * *

Karen Tox -- Here are the HED reviews (Risk Assessment) to do acute tox based on Sodium Benzoate.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

December 8, 2005

MEMORANDUM

Subject: Data Package D315790
Benzoic Acid New Chemical Screen

From: Wallace Powell, Biologist
Product Science Branch
Antimicrobials Division (7510C)

Through: Karen P. Hicks, Team Leader
Chemistry/Toxicology Team
Product Science Branch
Antimicrobials Division (7510C)

Michele E. Wingfield, Chief
Product Science Branch
Antimicrobials Division (7510C)

To: Velma Noble, Product Manager, Team 31
Tracy Lantz, Team Reviewer, Team 31
Regulatory Management Branch I
Antimicrobials Division (7510C)

BACKGROUND

Petro-Canada wishes to register technical grade benzoic acid, 99.93% purity. Benzoic acid is a New Chemical active ingredient. Petro-Canada wishes to rely on acute toxicity data support for sodium benzoate in support of benzoic acid.

In a March 30, 2005 meeting between Petro-Canada and Antimicrobials Division representatives, the consensus opinion regarding acute toxicity data support was that new data for benzoic acid would most likely not be needed. It was thought that Petro-Canada could most likely rely on sodium benzoate data, either in general or at least in regard to acute oral toxicity.

DISCUSSION

A summary of available information on the toxicological effects of benzoic acid and sodium benzoate is found in a September 25, 2003 Health Effects Division (HED) document "Benzoic Acid and Benzoate salts: Health Effects Division Science Assessment Document for Tolerance

Reassessment." Regarding the similarity between the two chemicals, the HED document states that "it was considered that data gaps for one benzoate salt could be adequately addressed by the existing data for the other benzoate compounds. Benzoic acid and its salts are rapidly absorbed by mammals, conjugated with glycine, and rapidly excreted in the urine as hippuric acid."

The HED document also lists study results and their corresponding acute Toxicity Categories for benzoic acid and, where available, for sodium benzoate. Acute effects for which the Toxicity Categories are listed for both chemicals are acute oral toxicity, eye irritation, skin irritation, and skin sensitization. For these effects, with the exception of eye irritation, the Categories are in general agreement between the two chemicals, with benzoic acid showing slightly greater acute effect where there is a difference. For eye irritation, benzoic acid data showed severe irritation whereas sodium benzoate was non-irritating. This is not too surprising, however, since eye irritation is a particularly variable acute effect, from one substance to another. (Appropriately, the label for the proposed benzoic acid product indicates severe eye irritation.) Data for the other two acute effects -- acute dermal and acute inhalation toxicity -- are available for benzoic acid itself (though not necessarilty for sodium benzoate).

Other study results and human effects information cited in Hazardous Substances Data Bank (HSDB, available at http://toxnet.nlm.nih.gov) and elsewhere help attest to the acute oral toxicity Category III rating for the two chemicals and also suggest that benzoic acid itself, though irritating, is not expected to be corrosive to the eye, respiratory tract, or mucous membranes.

RECOMMENDATION

Based on the similarity between sodium benzoate and benzoic acid, and based on the acute toxicity data summaries for both chemicals in the above-referenced HED document, it can be reasonably concluded that no further acute toxicity data is needed for the registration of technical grade benzoic acid. (This, however, does not apply to future registrations of formulations or dilutions, which will need to be supported by their own product-specific data or by cited data conducted on similar products.) Concerns about data gaps -- acute dermal and acute inhalation toxicity -- for sodium benzoate are allayed by the availability of such data for benzoic acid itself. Additionally, the above-cited data support in general appears consistent with information cited in Hazardous Substances Data Bank and elsewhere regarding these chemicals' effects in humans.

The acute Toxicity Categories listed in the above-referenced HED document for benzoic acid are as follows:

Acute oral toxicity	III
Acute dermal tox.	III (as worst case based on a limit test)
Acute inhalation tox.	IV
Eye irritation	I
Skin irritation	III
Skin sensitization	Non-sensitizing

Based on the above acute Toxicity Categories, the proposed product label (version "12/1/2004 Draft") should be revised in accordance with the Label Review Manual as follows:

1. Change the signal word "CAUTION" to read "DANGER".

2. Add the statement "Harmful if absorbed through skin" (or add "if absorbed through skin" to the "Harmful if swallowed" sentence).

The term "Corrosive" need not be required on the label, since benzoic acid does not appear to be corrosive to the eye. (References: http://www.inchem.org/documents/cicads/cicads/cicad26.htm, http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~ws8XTG:1 .)

The applicant-proposed *If Swallowed* portion of the First Aid section includes the statement "Do not give any liquid to the person." Whereas, the usual statement as per the Label Review Manual is "Have person sip a glass of water if able to swallow." However, the applicant may use the proposed statement if the applicant considers it medically preferable.

Products placed in Toxicity Category I for eye irritation must normally include the following "Note to Physician" statment near the First Aid section: "Probable mucosal damage may contraindicate the use of gastric lavage." However, mucosal damage from benzoic acid is not expected, and the statement need not be required in this case unless the applicant considers it appropriate.

F I F R A

CONFIDENTIAL BUSINESS INFORMATION
DOES NOT CONTAIN
NATIONAL SECURITY INFORMATION (EO 12356)

Some information in the attached material may be entitled to treatment as trade secret or proprietary data section 7(d) and section 10 the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) as amended.

Any person handling or using the attached data in any way is responsible for preventing unauthorized disclosure while in his/her possession. Section 12(a)(2)(D) makes it unlawful for any employee to use to his/her own advantage or to reveal any confidential information (except to persons needing the information for the performance of official duties). A penalty of up to $10,000 fine and up 3 years imprisonment may result from conviction of a violation on section 12(a)(2)(D).

Section 10(f) makes it a crime for any employee to disclose confidential information except as authorized by section 7 and 10 of FIFRA. A penalty of up to $10,000 fine and up to one year in jail may result from conviction of a violation of section 10(f).

The attached information is not to be published, reproduced, publicly discussed, included in response to an FOI request or otherwise released without the explicit written authorization of the appropriate division or his designee.

Page 48 contains the product confidential statement of formula and is not included in this copy.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

September
~~August~~ 29, 2003

MEMORANDUM

SUBJECT: Tolerance Reassessment Decisions Completed by the Lower Toxicity Pesticide Chemical Focus Group

FROM: Peter Caulkins, Associate Director
Registration Division

TO: Richard Keigwin, Acting Associate Director
Special Review and Reregistration Division

Please find attached the Focus Group Decision Document for benzoic acid and its sodium salt. The four tolerance exemptions for these chemicals in 40 CFR 180.1001 are reassessed.

If you have any comments or questions, please contact Kathryn Boyle at 703-305-6304.

Attachments (1)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

September 27, 2003

MEMORANDUM

FROM: Kathryn Boyle, Chair
Lower Toxicity Pesticide Chemical Focus Group
Registration Division

TO: Susan Lewis, Acting Chief
Minor Use, Inerts, and Emergency Response Branch
Registration Division

SUBJECT: Recommendation for Tolerance Reassessment

The attached science assessment discusses the toxicity of benzoic acid and its sodium, potassium, calcium, ammonium, and magnesium salts. Based on the rapid metabolism and excretion of these chemicals, and the existing assessments, a qualitative assessment was performed.

Based on its review and evaluation of the available information, EPA concludes that there is a reasonable certainty that no harm will result to the general population, and to infants and children from aggregate exposure to residues of benzoic acid and its sodium, potassium, calcium, ammonium, and magnesium salts from their uses as inert ingredients in pesticide products. The benzoic acid exemptions from the requirement of a tolerance as established in 40 CFR 180.1001 (c) and (e) and the sodium benzoate exemptions from the requirement of a tolerance as established in 40 CFR 180.1001 (c) and (e) are reassessed. Based on their rapid metabolism and excretion and the available information on acute toxicity, sodium, potassium, calcium, ammonium, and magnesium benzoate are reclassified as List 4A. Benzoic acid is classified as List 4B based on severe eye irritation (Toxicity Category I).

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

September 25, 2003

Memorandum

Subject: Benzoic Acid and Benzoate salts: Health Effects Division Science Assessment Document for Tolerance Reassessment.

CAS No.:	65-85-0	(benzoic acid)
	532-32-1	(sodium benzoate)
	582-25-2	(potassium benzoate)
	2090-05-3	(calcium benzoate)
	1863-63-4	(ammonium benzoate)
	563-70-8	(magnesium benzoate)
Chemical Class:		benzoates

From: Elissa Reaves, Toxicologist
Reregistration Branch 2
Health Effects Division (7509C)

Through: Pauline Wagner, Branch Chief
Reregistration Branch 2
Health Effects Division (7509C)

To: Lower Toxicity Pesticide Chemical Focus Group
Kathryn Boyle, Chair
Registration Division (7505C)

Background:

Attached is the Lower Toxicity Pesticide Chemicals Focus Group's science assessment for benzoic acid, sodium benzoate, and other salts of benzoic acid. This assessment summarizes available information on the use, physical/chemical properties, toxicological effects, and exposure profile of these benzoate salts. In performing this assessment, EPA has utilized reviews previously performed by EPA and FDA and relied on peer-reviewed evaluations performed by the Cosmetic Ingredient Review (CIR) and FAO/WHO.

I. Executive Summary:

Benzoic acid, also called benzenecarboxylic acid, occurs naturally in certain foods such as raspberries, cranberries, prunes, cinnamon, ripe cloves, plums, tea, anise, and oil of lovage; with most berries containing about 0.05 percent. Benzoic acid and sodium benzoate have been used for decades in pharmaceuticals, as a pH adjustor and/or preservative in cosmetics, bath and beauty products, and as preservatives/ antimicrobial agents in foods and beverages. Less is known about the other salt forms of benzoic acid (ammonium, calcium, magnesium, and potassium). However, it was considered that data gaps for one benzoate salt could be adequately addressed by the existing data for the other benzoate compounds. Benzoic acid and its salts are rapidly absorbed by mammals, conjugated with glycine, and rapidly excreted in the urine as hippuric acid. There is no reported accumulation of benzoate in the body. However, the ability to conjugate benzoic acid depends upon adequate liver function and nutritional supply of glycine.

Toxicological effects from exposure to benzoate solids documented in various websites and from open literature studies include irritation to the nose and throat, slight to moderate irritation to the skin, and irritation to the eyes. The benzoates were recognized to produce nonimmunologic contact reaction, but it was not determined whether the reactions were histamine or prostaglandin mediated. Dermal sensitization, photo toxicity, and photosensitization studies were negative.

The available ecotoxicity data for benzoic acid and the benzoate salts indicate that these compounds are expected to be readily biodegradable in the environment, are of low toxicity to fish and other aquatic organisms, mammals, and birds. EPA believes that benzoic and the benzoate salts will not cause unreasonable adverse effects on the environment.

Based on available information on benzoic acid and benzoate salts, their natural occurrence in berries, their expected use patterns, their safe history of use as food additives, their extensive use in cosmetics and bath products, and their low toxicity, the Health Effects Division (HED) has determined that a quantitative risk assessment is not warranted for these compounds.

II. Use Information:

The tolerance exemptions being reassessed in this document, the 40 CFR location of the established tolerance exemption, and the use pattern as an inert or active ingredient are listed in

Table 1.

Table 1. *Use Pattern (pesticidal-inert ingredient)*

Chemical Name	PC Code	40 CFR 180.1001 ◊	Inert Use Pattern (Pesticidal)	Current Inert List*
Benzoic Acid	809101	(c) (e)	preservative for formulations	4B
Sodium Benzoate	809103	(c) (e)	anticaking agent, stabilizer, preservative	4B
Potassium Benzoate	709103		non-food only	--
Calcium Benzoate	900653		non-food only	3
Ammonium Benzoate	809099		non-food only	3
Magnesium Benzoate	900323		non-food only	3

◊Residues listed in section (c) of 40 CFR 180.1001 are exempted from a tolerance when used as inert ingredients in pesticide formulations when applied to growing crops or to raw agricultural commodities after harvest; residues listed in section (e) of 40 CFR 180.1001 are exempted from a tolerance when used as inert ingredients in pesticide formulations applied to animals.
*Inert ingredients are categorized into four lists as described in the 52 FR 13305, Inert Ingredients in Pesticide Products Policy Statement. List 3 includes inert ingredients of unknown toxicity. Inert ingredients on this list have not yet been determined to be of minimal concern. List 4 are inert ingredients of minimal concern and are subdivided into 4A (minimal risk inert ingredients) and 4B (inert ingredients with sufficient data to substantiate safe use in pesticide products).
NA Not available

According to the OPPIN database, both benzoic acid and sodium benzoate also have active ingredient PC Codes, 009101 and 009103, respectively. There are no active or pending registrations for benzoic acid as an active ingredient, and only one active registration for sodium benzoate.

Use Pattern (non-pesticidal):

Benzoic Acid: Benzoic acid is generally recognized as safe (GRAS) by the U.S. FDA when used as an antimicrobial and flavoring agent and adjuvant (21 CFR 184.1021). The ingredient is used in food levels not to exceed good manufacturing practice with a maximum usage level of 0.1% in food. Benzoic acid and sodium benzoate are also used as a preservative in cosmetic formulations with the majority of both ingredients used at <1% (Anderson 2001). Benzoic acid and sodium benzoate are both also used as a pH adjustor and/or preservative in bath and body products, and in pharmaceuticals. The major outlet (75%) for the production of benzoic acid is as a chemical intermediate in the production of phenol. Other uses of benzoic acid not specifically regulated includes the use in paints, varnishes, solvents, cleaning and washing agents, photo chemicals and antifreeze agents.

The Agency notes that benzoic acid is included on the Agency's list of chemicals included in the High Production Volume (HPV) Challenge Program. HPV chemicals are those

that are manufactured or imported into the United States in volumes greater than one million pounds per year. There are approximately 3,000 HPV chemicals that are produced or imported into the United States. The HPV Challenge Program is a voluntary partnership between industry, environmental groups, and the EPA which invites chemical manufacturers and importers to provide basic hazard data on the HPV chemicals they produce/import. The goal of this program is to facilitate the public's right-to-know about the potential hazards of chemicals found in their environment, their homes, their workplace, and in consumer products.

Sodium Benzoate: Sodium benzoate is generally recognized as safe by the U.S. FDA when used as an antimicrobial and flavoring agent and adjuvant (21 CFR 184.1733). The ingredient is used in food at levels not to exceed good manufacturing practice with a maximum usage level of 0.1% in food. The Cosmetic Ingredient Review (CIR) Expert Panel concluded that benzoic acid and sodium benzoate could be used safely in cosmetic formulations at concentrations up to 5% (Anderson 2001). Sodium benzoate is mainly produced for use as a preservative in food and beverages (60%) and is also important for use in cooling liquids (10%). The use of sodium benzoate in paint strippers is limited to uses in industrial settings. Other uses of sodium benzoate may include the use in paints, varnishes, solvents, cleaning and washing agents, photo chemicals, and antifreeze agents. The Agency notes that sodium benzoate is included on the HPV Challenge Program.

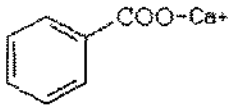
Ammonium Benzoate (Benzoic Acid NH_{4+}): Ammonium benzoate is regulated by the U.S. FDA as an indirect food additive for the limited use as a preservative component of adhesives (21 CFR 175.105). Ammonium benzoate is also reported as an industrial preservative for paper wrappers and as an agent for reducing curing time in vulcanization of rubber. Ammonium benzoate is not currently being sponsored; however, it is within the scope of the HPV Challenge Program and is currently available for sponsorship.

III. Physical/Chemical Properties:

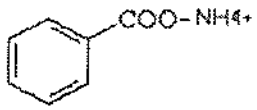
Table 2. Physical/Chemical Properties.

	Benzoic Acid	**Sodium Benzoate***	**Benzoic Acid NH_{4+}**
Physical State	white solid	white solid	white solid
Molecular Formula	C_6H_5COOH	$C_6H_5COONa+$	$C_6H_5COONH_{4+}$
Molecular Weight (Da)	122.12	144.11	139.16
Melting Point °C	122.4	330.6	198
Water Solubility	insoluble	soluble	soluble
Density (g/cm^3)	1.2659	1.44	1.260

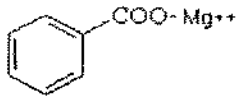
* Data for magnesium benzoate, potassium benzoate or calcium benzoate are expected to be similar to sodium benzoate.



Calcium Benzoate



Ammonium Benzoate



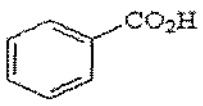
Benzoic Acid Mg++

IV. Hazard Assessment

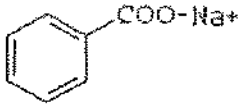
Table 3. Summary of Acute Toxicity Data on Benzoic Acid and Sodium Benzoate.

Benzoic Acid				Sodium Benzoate		
Test	**Species**	**Results**	**Category**	**Species**	**Results**	**Category**
Oral LD_{50}	rat	2565 mg/kg	III	rat	3140 mg/kg	III
Dermal LD_{50}	rabbit	>2000 mg/kg	III		no data	
Inhalation LC_{50}	rat	>12.2 mg/l/4h.	IV		no data	
Eye Irritation	rabbit	severe irritation	I	rabbit	slightly irritating	III
Dermal Irritation	rabbit	non to slightly irritating	III	rabbit	non-irritating	IV
Dermal Sensitization	guinea pig	not sensitizing	Not applicable	human	nonimmunologic contact urticaria	Not applicable

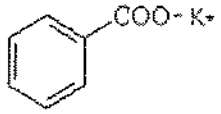
A. Toxicological Profile: The general effects of exposure to benzoic acid and sodium benzoate or its salts include nose and throat irritation if inhaled, as well as slight skin and severe eye irritation. Benzoic acid and the benzoate salts are rapidly metabolized and excreted, do not bioaccumulate, and have low toxicity after acute and repeated exposures. Early human consumption studies indicated no externally visible effects from ingesting 0.5 to 1.0 g/day of benzoic acid for 44 consecutive days or for 82/86 or 88/92 days (Gerlach 1909; as cited in USEPA IRIS). Assuming a human body weight of 70 kg, this corresponds to a dose of 14 mg/kg/day of benzoic acid. In another early study (1909), men who drank from 1 to 2.5 liters of apple juice containing 0.1 percent sodium benzoate complained of burning taste, headache, nausea and vomiting, itching of the skin, sweating, constipation and albuminuria. However, massive doses of sodium benzoate (25-60 g per day) were given to rheumatic patients without producing any harmful effects (FDA 1973). Adverse effects in humans given an oral



Benzoic Acid



Sodium Benzoate



Potassium Benzoate

bolus dose of less than or equal to 1.75 g/day of benzoic acid over a 20-day period include observed irritation, discomfort, weakness, and malaise (Wiley and Bigelow 1908; as cited in USEPA IRIS).

The oral LD_{50} for benzoic acid is 1,520 mg for the rabbit and 2,000 mg for the cat and dog. The lethal dose for benzoic acid in sheep is estimated to be 1,000 mg/kg (FDA 1973).

A chronic oral dose of 40 mg/kg/day of benzoic acid for 17 months was associated with decreased resistance to stress in mice and possibly with reduced food and water intake in rats after 18 months. However, another study reported by the same laboratory indicated 80 mg/kg/day in rats for 18 months was not associated with adverse effects on body weight, survival, or gross or microscopic pathology (Shtenberg and Ignat'er 1970; Ignat'er 1965; as cited in USEPA IRIS). Other long-term dietary studies showed decreased food intake and body weight in rats fed 1.5% benzoic acid (750 mg/kg/day). A reduced dose of 1.0% benzoic acid in the diet (50 mg/kg/day) did not produce signs of toxicity or adverse reproductive effects (Marquardt 1960; as cited in USEPA IRIS).

No positive results have been reported for benzoic acid or sodium benzoate when tested for mutagenicity or genotoxicity in prokaryotes, eukaryotes, and several mammalian test systems (McCann et al., 1975; Litton Bionetics, Inc., 1975 and 1975; Oikawa et al., 1980; as cited in USEPA IRIS).

B. Cations: Ammonium, Calcium, Magnesium, Potassium, and Sodium:

Calcium: The human body burden of calcium is approximately 1 kg for a 70 kg adult; this, 1/70th of our weight is calcium. The calcium cation is necessary for bone and teeth formation. It is also important to the proper functioning of nerves, enzymes, and muscles, and plays a role in blood clotting and the maintenance of cell membranes. The recommended daily allowances (RDAs) for calcium are 1000 mg/day for adults aged 19 to 50 years, and 1200 mg/day for individuals older than 50 years.

Magnesium: The human body burden of magnesium is approximately 20 g for a 70 kg adult. The magnesium cation is also used in building bones. It plays a role in releasing energy from muscles and regulating body temperature. The RDA is 310 to 320 mg/day for adult females, and 400 to 420 mg/day for adult males, with the RDA increasing with increasing age.

Potassium: The human body burden of potassium is approximately 140 g for a 70 kg adult. The potassium cation is important in regulating blood pressure, regulating cellular water content, maintaining proper pH balance, and transmission of nerve impulses. It helps to regulate the electrical activity of the heart and muscles. The potassium RDA is 900 mg/day.

Sodium: The human body burden of sodium is approximately 20 g for a 70 kg adult. The sodium cation is necessary for the nerves and muscles to function properly. It is the principal cation of extracellular fluid, and helps to maintain the body's water balance. These electrolytes,

the electrically charged ions in the body fluids, consist to a great extent of sodium and potassium. There is no Recommended Daily Allowance (RDA) for sodium.

C. Ammonium Salt:

Ammonium salts dissociate to the negatively charged anion and the positively charged ammonium cation (NH_4^+). Humans cannot convert atmospheric nitrogen to any form that can be used as part of any of the various metabolic cycles. Therefore, reduced nitrogen (NH_4^+) has to enter the body from an outside source. These sources are the nitrogen-containing amino acids in protein which are consumed daily as part of the diet. Although the human body can produce some amino acids, ten amino acids are considered "essential" amino acids, i.e., they must be consumed in the diet.

Generally the body works to maintain a balance of nitrogen intake and nitrogen excretion. The estimated daily ammonia intake through food and drinking water is 18 mg. In contrast, 4000 mg of ammonia per day are produced endogenously in the human intestine.

Ammonia and the ammonium ion are integral components of normal human metabolic processes. Ammonia is released following deamination that occurs when protein is used by the body for energy production. The liver converts ammonia via the urea cycle into urea. According to FDA in the "Evaluation of the Health Aspects of Certain Ammonium Salts as Food Ingredients" (1974), "the normal liver so readily detoxifies ammonium ion from alimentary sources that blood concentrations of ammonium salts do not rise to the levels necessary to evoke toxic response." Approximately 80% of the body's excess nitrogen is eliminated through the kidneys as urea, approximately 25 to 30 grams per day.

D. Special Considerations for Infants and Children

Given the wide spread occurrence of benzoates in the food supply, the amount of benzoates that can be applied to food as a result of its use in a pesticide product should not significantly increase the existing amounts in the food supply. Oral doses of sodium benzoate appeared to have no maternal toxicity, fetal toxicity, or teratogenicity in mice, rats, hamsters, or rabbits with the highest doses tested being 175.0 mg/kg/day in mice and rats, 300.0 mg/kg/day in hamsters, and 250.0 mg/kg/day in rabbits (FDRL 1972; as cited in USEPA IRIS).

However, there is some concern that low birth weight or premature infants with immature livers can experience adverse effects when administered benzoic acid or benzoate salts. Infants with immature livers may not be capable of metabolizing benzoate. It was suggested that a combination of sodium benzoate and sodium phenylacetate not be administered to low birth weight infants unless the benefits outweigh the risks (AMA 1991; USP DI 1992, as cited in TOXNET).

EPA believes there would be a very low exposure of premature or very young infants to

benzoates. First, premature or very young infants ingest only formula or breast milk. (It is generally recommended that infants not consume solid food until 4 to 6 months of age.) Regulation of infant formulas is under the purview of the FDA. (www.fda.gov/fdac/features/596_baby.html). Benzoic acid and sodium benzoate are generally recognized as safe (GRAS) under 21 CFR 184.1021 and 184.1733, respectively. Therefore, infants consuming only infant formula or breast milk would be exposed to very low amounts of benzoates. Second, even if a young infant were to be fed some solid food, given the characteristics of benzoic acid and benzoate salts, residues are not likely to be present above naturally occurring concentrations. As discussed below (section 7) the benzoates are readily biodegradable. It is not likely to be taken up by plants.

Once past this several month time-period, there is no longer a concern for potential sensitivity to infants and children. Older infants, like adults, process benzoates through well understood metabolic pathways. A safety factor analysis has not been used to assess the risk. For the same reasons the additional tenfold safety factor is unnecessary.

V. Exposure Assessment

Benzoic acid and sodium benzoate have been used for decades in pharmaceuticals, cosmetics and/or in food as preservatives and flavoring/fragrance agents. According to information in Product Registers the substances are also used in different kinds of products, such as in paints, varnishes, solvents, cleaning and washing agents, photo chemicals, and antifreeze agents. Benzoic acid and sodium benzoate both have the status "generally recognized as safe" (GRAS) by the U.S. FDA. An estimated daily food input of benzoate by the U.S. EPA was 278 mg as sodium benzoate and 34 mg as benzoic acid. (USEPA 1987; as cited in USEPA IRIS). In 1983, the Joint Expert Committee on Food Additives (JEFCA) of the World Health Organization (WHO) established a group acceptable daily intake (ADI) for benzoic acid and its salt of 5 mg/kg body weight. This group ADI is based on the structural similarity and common metabolic fate of these chemicals (WHO 1997).

The National Research Council subcommittee also provided a possible daily human intake of benzoic acid and sodium benzoate in the total diet based on a comprehensive survey. The following table summarizes the possible daily intake for individuals in various age groups (FDA 1973).

Table 4. Possible daily intake

	Total Intake mg				mg/ kilogram of body weight*			
	Benzoic Acid		**Sodium Benzoate**		**Benzoic Acid**		**Sodium Benzoate**	
Age group	Avg.	Max.	Avg.	Max	Avg.	Max.	Avg.	Max.
0-5 mos.	0.6	1	10	21	.1	.2	2	4
6-11 mos.	6	21	111	313	.8	2.6	14	39
12-23 mos.	16	46	188	404	1.4	4.2	17	37

2-65+ yrs.	34	87	328	669	0.6	1.4	5.5	11

* Calculations based on an average weight of 60 kg for an adult and the following estimated weights of infants by age groups: 0-5 mos., 5 kg; 6-11 mos., 8 kg; and 12-23 mos., 11 kg.

It should also be noted that the NRC subcommittee stated the calculations of benzoate intakes are likely over stated, possibly by considerable margins. The Select Committee regarded the figures given in the table as levels that would unlikely be consumed by any of the age groups. Figures in the table were considered to be generous overestimates of the benzoic acid and sodium benzoate content of the human diet (FDA 1973).

The worldwide production capacity for benzoic acid is estimated at 700 kt. The major outlet (75% or 525 kt) for benzoic acid is for the production of phenol, which in turn is mainly used to produce caprolactam. The next biggest outlet is as a feedstock for sodium benzoate (10% or 70 kt) and chemical synthesis of plasticizers (5% or 35 kt). So, benzoic acid is mainly used in controlled industrial settings.

The worldwide production of sodium benzoate is estimated at 100 kt. The major use for sodium benzoate is as a preservative in food and beverages (60% or 60 kt). The second most important market for sodium benzoate is for cooling liquids (10% or 10 kt). Like sodium benzoate, potassium benzoate is used mainly as a preservative in nonalcoholic beverages with an estimated worldwide production capacity of only 7 kt. Ammonium benzoate is approved only as an indirect food additive for use only as component of adhesives (21 CFR 175.105). No production estimates could be determined for ammonium benzoate or any of the other benzoate salts.

The use of benzoic acid and sodium benzoate in pesticide products as inert ingredients is expected to result in much lower exposure than the FDA-regulated use of these compounds, as well as lower exposure than in the average daily intake of benzoates. Therefore, a quantitative screening-level exposure assessment has not been conducted.

VI. Risk Characterization

Benzoic acid is a naturally occurring compound found in berries and other foods. As previously discussed in this document, there are many FDA approved uses for benzoic acid and the benzoate salts. Residues from the pesticide uses of the benzoates are not likely to greatly contribute to the levels already approximated as the average daily intake.

As noted previously, three of the benzoates assessed in this document, benzoic acid, sodium benzoate, and ammonium benzoate, are included on the Agency's list of chemicals included in the High Production Volume (HPV) Challenge Program. HPV chemicals are those that are manufactured or imported into the United States in volumes greater than one million pounds per year. There are approximately 3,000 HPV chemicals that are produced or imported into the United States. The HPV Challenge Program is a voluntary partnership between industry, environmental groups, and the EPA which invites chemical manufacturers and importers to

provide basic hazard data on the HPV chemicals they produce/import. The goal of this program is to facilitate the public's right-to-know about the potential hazards of chemicals found in their environment, their homes, their workplace, and in consumer products. Based on the available toxicity data for the benzoates, the Agency feels confident in proceeding with this tolerance reassessment decision. Any submission of data by sponsors of benzoic acid, sodium benzoate, and ammonium benzoate as part of the HPV Challenge Program may, in the future, be used by OPP to revise or update their tolerance reassessment decision for these benzoates as deemed necessary and appropriate.

Taking into consideration all available information on benzoic acid, sodium benzoate, and the other salts of benzoate, including the FDA's designation of GRAS for benzoic acid and sodium benzoate, as preservatives/antimicrobial agents in foods and beverages, the historical use of benzoic acid and sodium benzoate in pharmaceuticals, cosmetics, as well as the natural presence of benzoic acid in berries, the use of ammonium benzoate as a preservative in adhesive components in foods, the use of benzoic acid and the benzoate salts as inert ingredients in pesticide formulations are unlikely to pose a significant hazard to the general public or any population subgroup. Therefore, HED is conducting a qualitative approach to assessing human health risks from exposure to benzoates.

VII. Environmental Fate/Ecotoxicity/Drinking Water Considerations:

The environmental fate and occurrence of benzoic acid has been well studied. The Hazardous Substances Database (HSDB) (www.toxnet.nlm.nih.gov) contains extensive summaries of the environmental fate of benzoic acid. In addition, HSDB information has been supplemented with predictive modeling based on structure activity relationships. For this analysis, sodium, potassium calcium, and magnesium salts were considered equivalent with respect to their environmental fate and ecotoxicity. Slight differences in physical-chemical properties were observed, but are not expected to impact their behavior or toxicity in the environment. Benzoic acid and the ammonium salt of benzoic acid were addressed separately.

Table 1 provides key fate and chemical properties for benzoic acid and representative molecules of the salts. With a pKa of 4.204, benzoic acid will dissociate to form an anion at environmental pH up to the limits of its solubility. The benzoate salts are highly water soluble and readily dissociate into the anion (benzoic acid) and cation (sodium, potassium, calcium, magnesium and ammonium ion). Thus, the environmental fate and effects of the benzoic acid salts are closely related to that of benzoic acid, and the free cation.

Table 1. Properties and Environmental Fate of Benzoic Acid and Selected Salts

Property	Benzoic Acid	Sodium Benzoate	Benzoic Acid, Ammonium Salt
Water Solubility (mg/L) @ 25C	3400 (M)	5.56E05 (M)	>1.0E06 (E)

Vapor Pressure mm Hg @ 25C	7E-04 (M)	3.67E-09 (E)	2.65E-07 (E)
Henry's Law Coefficient (atm-m^3/mole)	3.8E-08 (M)	1.09E-07 (E)	5.2E-16 (E)
Biodegradation	Primary: hours-days Ultimate: days-weeks	Primary: hours-days Ultimate: days-weeks	Primary: hours-days Ultimate: days-weeks
Log K_{ow}	1.87 (M)	-2.27 (E)	-1.33 (E)
K_{oc} (ml/g)	14 (E)	14 (E)	99
Hydrolysis Half-life @pH 7 (days)	No hydrolizable functional groups	No hydrolizable functional groups	52 days

M: Measured; E: Estimated

Based on low K_{oc}s and log K_{ow}s, benzoic acid and its salt are classified as highly mobile in soil (McCall). Volatilization from water would be minimal, based on both benzoic acid and the salts' low Henry's Law constant. All compounds have a low potential to volatilize from soil surfaces, based on vapor pressures of less than 1×10^{-4} mm Hg.

The biodegradability of benzoic acid has been extensively studied and are expected to be readily biodegradable in the environment. Using both unacclimated and acclimated sludge inoculums, benzoic acid degraded with half-lives of less than approximately 5 days. In most all cases, near complete mineralization occurred in under 10 days. In soil inoculums, benzoic acid exhibited a half-life for mineralization of 4.5 hours. In a second study, complete mineralization occurred in one day. Benzoic acid degraded in a polluted river water in 0.85 days and in reservoir water in 3.6 days. Degradation appears to be concentration dependent, with low concentrations, less than 1 ppb, mineralizing in eutrophic and oligotrophic lake water in under 7 days. Overall half-lives in unacclimated and acclimated systems ranges from hours to days for primary degradation and hours to weeks for ultimate (mineralization) degradation.

In an acidic soil, benzoic acid mineralized up to 80 percent in less than 12 weeks. The same experiment in a neutral soil resulted in approximately 70 percent mineralized in 12 weeks. Anaerobically, more than 75 percent of benzoic acid mineralizes when incubated for 8 weeks using sludge from a secondary digester. In several other experiments using sewage sludge inoculums, benzoic acid mineralized >90 percent in as little as 7 to 18 days. In a study using anoxic sediment from a hypereutrophic lake in Kalamazoo, MI, benzoic acid degraded completely (methane and CO_2) in one week.

Due to the lack of hydrolyzable functional groups, abiotic degradation of benzoic acid and the salts of benzoate would not be expected to be an important fate process. However, the ammonium salt would hydrolyze in neutral to alkaline environments from 5 days at pH 8 to 52 days at pH 7. Benzoic acid is expected to photolyze based on UV adsorption at 310nm. Available data indicate that 10.2 percent photolyzes in approximately 17 hours.

If any of these compounds were to enter the atmosphere, it is expected to exist solely as a vapor. Vapor-phase benzoic acid would be readily degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicles with an estimated half-life of 8 days.

Estimated toxicity (Meylan, 1998) indicates benzoic acid is the most toxic of the substances reviewed in this assessment. Table 2 lists the estimated toxicity for several species. Green algae and fish are among the most sensitive species based on predictive modeling for acute and chronic endpoints for all compounds. Based on the environmental fate profile of benzoic acid and its salts, exposures from labels uses are unlikely to reach concentrations necessary to elicit effects in aquatic organisms. Using laboratory rat data as a surrogate for terrestrial wild mammals and birds, benzoic acid and its salts do not appear to be very toxic and adverse effects from labeled uses is not expected.

Table 2. Ecotoxicity of Benzoic Acid and Selected Salts

Property	Benzoic Acid	Sodium Benzoate	Benzoic Acid, Ammonium Salt
Fish (96-h LC_{50}; mg/L)	1200	>1.0E06	1.4E05
Daphnid (48-h LC_{50}; mg/L)	1274	8.8E05	1.2E05
Green Algae (96-h EC_{50}; mg/L)	790	4.3E05	61172
Fish (30-day Chronic; mg/L)	151	71380	10486
Fish (SW) (96-h LC_{50}; mg/L)	258	32047	6374
Mysid Shrimp (96-h LC_{50}; mg/L)	380	>1.0E06	4.3E05
Green Algae (96-h Chronic; mg/L)	73	3646	893
Earthworm (14-day LC_{50}; mg/Kg dry wt.)	8238	18317	9081

Detections of benzoic acid in surface water have been extensively reported, but not quantified. In ground water, concentrations of <0.1 ppb have been reported for areas without known sources of potential contamination such as landfills, wood preserving facilities, and petroleum operations. Benzoic acid has been detected in the particulate fraction of rain and snow. In drinking water, concentrations of up to 15 ppm in the tap water of Ottumwa, IA was reported, but was not detected in water from utilities in Seattle, Philadelphia, or Cincinnati. Benzoic acid has been detected, but not quantified, in other drinking water monitoring studies, domestically and internationally. Overall, and with few exceptions, concentrations of benzoic acid in ambient and drinking water is expected to be in the low ppb range.

VIII. Cumulative Exposure:

Section 408(b)(2)(D)(v) of the FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."

EPA does not have, at this time, available data to determine whether benzoic acid or the benzoate salts have a common mechanism of toxicity with other substances. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to benzoic acid or the benzoate salts and any other substances and benzoic acid or the benzoate salts do no appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that benzoic acid or the benzoate salts have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

Refernees:

(Note to the Reader: MRID (Master Record Identification) Numbers were added to the references on October 17, 2003 and November 21, 2003. These numbers were not available at the time of document signature. No other changes were made to the document.)

AMA 1991. American Medical Association. AMA Drug Evaluations Annual 1991. Chicago, IL: American Medical Association, 1991. 2034

Anderson, F. Alan 2001. Forty-Fourth Report of the Cosmetic Ingredient Review Expert Panel. Final Report on the Safety Assessment of Benzyl Alcohol, Benzoic Acid, and Sodium Benzoate. (F. Alan Anderson). International Journal of Toxicology. Vol 20: Suppl 3: Pp 23-50. (MRID No. 46067601)

Department of Health and Human Services, National Institutes of Health, U.S. National Library of Medicine. Benzoic Acid; CAS Registry Number 65-85-0, Sodium Benzoate; CAS Registry Number 532-32-1, and Ammonium Benzoate; CAS Registry Number 1863-63-4. Available at http://www.toxnet.nlm.nih.gov.

FDA (Food and Drug Administration). 1973. Evaluation of the Health Aspects of Benzoic Acid and Sodium Benzoate as Food Ingredients. DHEW, Washington, DC. Report No. SCOGS-7. NTIS PB-223837/6. (MRID No. 46069301)

FDRL (Food and Drug Research Labs., Inc.). 1972. Teratologic Evaluation of FDA 71-37

(Sodium Benzoate). p.\75-79.

Gerlach, V. 1909. VII. Summary of the results. In: Physiological Activity of Benzoic Acid and Sodium Benzoate, V. Gerlach, Ed. Verlag von Heinrich Staadt, Wiesbaden. p.\90-92. (Cited in Informatics, Inc., 1972)

HSDB 2003. Hazardous Substances Database in http://www.toxnet.nlm.nih.gov

Ignat'ev, A.D. 1965. Experimental information contributing to a hygienic characterization of the combined effect produced by some food presentations. Vop. Pitan. 24(3): 61-68. (Cited in Informatics, Inc., 1972)

Litton Bionetics, Inc. 1974. Mutagenic Evaluation of Compound FDA 71-37, Sodium Benzoate. Report No. LBI 2446-297, FDA, Washington, DC, PB-245-453/6.

Litton Bionetics, Inc. 1975. Mutagenic Evaluation of Compound FDA 73-70, Benzoic Acid Certified A.C.S. Report No. LBI-2468-376; FDABF-GRAS-376 PB-245- 500/4.

McCall. McCall, P.J., D.A. Laskowski, R.L. Swann, H.J. Dishburger, "Measurements of Sorption Coefficients of Organic Chemicals on their use in Environmental Fate Analysis, Agricultural Products Department, Dow AgroChemicals USA, Midland, MI. P104 (89-109).

McCann, J., E. Choi, E. Yamasaki and B.N. Ames. 1975. Detection of carcinogens as mutagens in the Salmonella/microsome test: Assay of 300 chemicals. Proc. Natl. Acad. Sci. 72: 5135-5139.

Mylan, W. and P. Howard, 1998. ECOSAR Class Program, Version 0.99d. Syracuse Research Corporation, Syracuse, N.Y. For: U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, D.C.

Oikawa, A., H. Tohda, M. Kanai, M. Miwa and T. Sugimura. 1980. Inhibitors of poly(adenosine diphosphate ribose) induced sister chromatid exchanges. Biochem. Biophys. Res. Commun. 97(4): 1311-1316.

Shtenberg, A.J. and A.D. Ignat'ev. 1970. Toxicological evaluation of some combinations of food preservatives. Food Cosmet. Toxicol. 8(4): 369-380.

SIAR 2003. SIDS Initial Assessment Report. Benzoates Category. Pp1-34. (MRID 46107301, 46107501, 46107401, and 46107201)

USP DI 1992. US Pharmacopeia Dispensing Information; Drug Information for the Health Care

Professional 12th ed, V.1 p. 2475.

U.S. EPA. 1987. Health and Environmental Effects Document for Benzoic Acid. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA IRIS 2003. U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on Benzoic Acid (65-85-0). Available from: http://www.epa.gov/ngispgm3/iris/index.html

WHO 1997. World Health Organization. Technical Report Series 868. Evaluation of Certain Food Additives and Contaminants. Forty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Geneva. (1997)

Wiley, H.M. and W.D. Bigelow. 1908. Influence of benzoic acid and benzoates on digestion and health. Bulletin 84, pt. IV, Bureau of Chemistry, U.S. Dept. Agriculture. (Cited in Informatics, Inc., 1972)

Kathryn Boyle/DC/USEPA/US

11/22/2005 09:49 AM

To Tracy Lantz/DC/USEPA/US@EPA

cc

bcc

Subject benzoates

Tracy -

I was asked to send to you the document that was prepared on benzoic acid and its various salts. This document was the basis of the tolerance reassessment for the existing exemptions for benzoic acid and sodium benzoate. it will also be used in the near future to establish tolerance exemptions for the other salts which are now List 4A.

LTPC.Benzoic Acid.combo.wpd

Kathryn Boyle
Inert Ingredient Assessment Branch
Registration Division
Office of Pesticide Programs
703-305-6304

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

September
~~August~~ 29, 2003

MEMORANDUM

SUBJECT: Tolerance Reassessment Decisions Completed by the Lower Toxicity Pesticide Chemical Focus Group

FROM: Peter Caulkins, Associate Director
Registration Division

TO: Richard Keigwin, Acting Associate Director
Special Review and Reregistration Division

Please find attached the Focus Group Decision Document for benzoic acid and its sodium salt. The four tolerance exemptions for these chemicals in 40 CFR 180.1001 are reassessed.

If you have any comments or questions, please contact Kathryn Boyle at 703-305-6304.

Attachments (1)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

September 27, 2003

MEMORANDUM

FROM: Kathryn Boyle, Chair
Lower Toxicity Pesticide Chemical Focus Group
Registration Division

TO: Susan Lewis, Acting Chief
Minor Use, Inerts, and Emergency Response Branch
Registration Division

SUBJECT: Recommendation for Tolerance Reassessment

The attached science assessment discusses the toxicity of benzoic acid and its sodium, potassium, calcium, ammonium, and magnesium salts. Based on the rapid metabolism and excretion of these chemicals, and the existing assessments, a qualitative assessment was performed.

Based on its review and evaluation of the available information, EPA concludes that there is a reasonable certainty that no harm will result to the general population, and to infants and children from aggregate exposure to residues of benzoic acid and its sodium, potassium, calcium, ammonium, and magnesium salts from their uses as inert ingredients in pesticide products. The benzoic acid exemptions from the requirement of a tolerance as established in 40 CFR 180.1001 (c) and (e) and the sodium benzoate exemptions from the requirement of a tolerance as established in 40 CFR 180.1001 (c) and (e) are reassessed. Based on their rapid metabolism and excretion and the available information on acute toxicity, sodium, potassium, calcium, ammonium, and magnesium benzoate are reclassified as List 4A. Benzoic acid is classified as List 4B based on severe eye irritation (Toxicity Category I).

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

September 25, 2003

Memorandum

Subject: Benzoic Acid and Benzoate salts: Health Effects Division Science Assessment Document for Tolerance Reassessment.

CAS No.:	65-85-0	(benzoic acid)
	532-32-1	(sodium benzoate)
	582-25-2	(potassium benzoate)
	2090-05-3	(calcium benzoate)
	1863-63-4	(ammonium benzoate)
	563-70-8	(magnesium benzoate)
Chemical Class:		benzoates

From: Elissa Reaves, Toxicologist
Reregistration Branch 2
Health Effects Division (7509C)

Through: Pauline Wagner, Branch Chief
Reregistration Branch 2
Health Effects Division (7509C)

To: Lower Toxicity Pesticide Chemical Focus Group
Kathryn Boyle, Chair
Registration Division (7505C)

Background:

Attached is the Lower Toxicity Pesticide Chemicals Focus Group's science assessment for benzoic acid, sodium benzoate, and other salts of benzoic acid. This assessment summarizes available information on the use, physical/chemical properties, toxicological effects, and exposure profile of these benzoate salts. In performing this assessment, EPA has utilized reviews previously performed by EPA and FDA and relied on peer-reviewed evaluations performed by the Cosmetic Ingredient Review (CIR) and FAO/WHO.

I. Executive Summary:

Benzoic acid, also called benzenecarboxylic acid, occurs naturally in certain foods such as raspberries, cranberries, prunes, cinnamon, ripe cloves, plums, tea, anise, and oil of lovage; with most berries containing about 0.05 percent. Benzoic acid and sodium benzoate have been used for decades in pharmaceuticals, as a pH adjustor and/or preservative in cosmetics, bath and beauty products, and as preservatives/ antimicrobial agents in foods and beverages. Less is known about the other salt forms of benzoic acid (ammonium, calcium, magnesium, and potassium). However, it was considered that data gaps for one benzoate salt could be adequately addressed by the existing data for the other benzoate compounds. Benzoic acid and its salts are rapidly absorbed by mammals, conjugated with glycine, and rapidly excreted in the urine as hippuric acid. There is no reported accumulation of benzoate in the body. However, the ability to conjugate benzoic acid depends upon adequate liver function and nutritional supply of glycine.

Toxicological effects from exposure to benzoate solids documented in various websites and from open literature studies include irritation to the nose and throat, slight to moderate irritation to the skin, and irritation to the eyes. The benzoates were recognized to produce nonimmunologic contact reaction, but it was not determined whether the reactions were histamine or prostaglandin mediated. Dermal sensitization, photo toxicity, and photosensitization studies were negative.

The available ecotoxicity data for benzoic acid and the benzoate salts indicate that these compounds are expected to be readily biodegradable in the environment, are of low toxicity to fish and other aquatic organisms, mammals, and birds. EPA believes that benzoic and the benzoate salts will not cause unreasonable adverse effects on the environment.

Based on available information on benzoic acid and benzoate salts, their natural occurrence in berries, their expected use patterns, their safe history of use as food additives, their extensive use in cosmetics and bath products, and their low toxicity, the Health Effects Division (HED) has determined that a quantitative risk assessment is not warranted for these compounds.

II. Use Information:

The tolerance exemptions being reassessed in this document, the 40 CFR location of the established tolerance exemption, and the use pattern as an inert or active ingredient are listed in

Table 1.

Table 1. *Use Pattern (pesticidal-inert ingredient)*

Chemical Name	PC Code	40 CFR 180.1001 ◊	Inert Use Pattern (Pesticidal)	Current Inert List*
Benzoic Acid	809101	(c) (e)	preservative for formulations	4B
Sodium Benzoate	809103	(c) (e)	anticaking agent, stabilizer, preservative	4B
Potassium Benzoate	709103		non-food only	--
Calcium Benzoate	900653		non-food only	3
Ammonium Benzoate	809099		non-food only	3
Magnesium Benzoate	900323		non-food only	3

◊Residues listed in section (c) of 40 CFR 180.1001 are exempted from a tolerance when used as inert ingredients in pesticide formulations when applied to growing crops or to raw agricultural commodities after harvest; residues listed in section (e) of 40 CFR 180.1001 are exempted from a tolerance when used as inert ingredients in pesticide formulations applied to animals.

*Inert ingredients are categorized into four lists as described in the 52 FR 13305, Inert Ingredients in Pesticide Products Policy Statement. List 3 includes inert ingredients of unknown toxicity. Inert ingredients on this list have not yet been determined to be of minimal concern. List 4 are inert ingredients of minimal concern and are subdivided into 4A (minimal risk inert ingredients) and 4B (inert ingredients with sufficient data to substantiate safe use in pesticide products).

NA Not available

According to the OPPIN database, both benzoic acid and sodium benzoate also have active ingredient PC Codes, 009101 and 009103, respectively. There are no active or pending registrations for benzoic acid as an active ingredient, and only one active registration for sodium benzoate.

Use Pattern (non-pesticidal):

Benzoic Acid: Benzoic acid is generally recognized as safe (GRAS) by the U.S. FDA when used as an antimicrobial and flavoring agent and adjuvant (21 CFR 184.1021). The ingredient is used in food levels not to exceed good manufacturing practice with a maximum usage level of 0.1% in food. Benzoic acid and sodium benzoate are also used as a preservative in cosmetic formulations with the majority of both ingredients used at <1% (Anderson 2001). Benzoic acid and sodium benzoate are both also used as a pH adjustor and/or preservative in bath and body products, and in pharmaceuticals. The major outlet (75%) for the production of benzoic acid is as a chemical intermediate in the production of phenol. Other uses of benzoic acid not specifically regulated includes the use in paints, varnishes, solvents, cleaning and washing agents, photo chemicals and antifreeze agents.

The Agency notes that benzoic acid is included on the Agency's list of chemicals included in the High Production Volume (HPV) Challenge Program. HPV chemicals are those

that are manufactured or imported into the United States in volumes greater than one million pounds per year. There are approximately 3,000 HPV chemicals that are produced or imported into the United States. The HPV Challenge Program is a voluntary partnership between industry, environmental groups, and the EPA which invites chemical manufacturers and importers to provide basic hazard data on the HPV chemicals they produce/import. The goal of this program is to facilitate the public's right-to-know about the potential hazards of chemicals found in their environment, their homes, their workplace, and in consumer products.

Sodium Benzoate: Sodium benzoate is generally recognized as safe by the U.S. FDA when used as an antimicrobial and flavoring agent and adjuvant (21 CFR 184.1733). The ingredient is used in food at levels not to exceed good manufacturing practice with a maximum usage level of 0.1% in food. The Cosmetic Ingredient Review (CIR) Expert Panel concluded that benzoic acid and sodium benzoate could be used safely in cosmetic formulations at concentrations up to 5% (Anderson 2001). Sodium benzoate is mainly produced for use as a preservative in food and beverages (60%) and is also important for use in cooling liquids (10%). The use of sodium benzoate in paint strippers is limited to uses in industrial settings. Other uses of sodium benzoate may include the use in paints, varnishes, solvents, cleaning and washing agents, photo chemicals, and antifreeze agents. The Agency notes that sodium benzoate is included on the HPV Challenge Program.

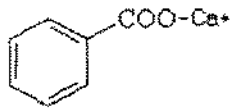
Ammonium Benzoate (Benzoic Acid NH_{4+}): Ammonium benzoate is regulated by the U.S. FDA as an indirect food additive for the limited use as a preservative component of adhesives (21 CFR 175.105). Ammonium benzoate is also reported as an industrial preservative for paper wrappers and as an agent for reducing curing time in vulcanization of rubber. Ammonium benzoate is not currently being sponsored; however, it is within the scope of the HPV Challenge Program and is currently available for sponsorship.

III. Physical/Chemical Properties:

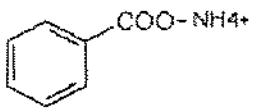
Table 2. Physical/Chemical Properties.

	Benzoic Acid	**Sodium Benzoate***	**Benzoic Acid NH_{4+}**
Physical State	white solid	white solid	white solid
Molecular Formula	C_6H_5COOH	$C_6H_5COONa+$	$C_6H_5COONH_{4+}$
Molecular Weight (Da)	122.12	144.11	139.16
Melting Point °C	122.4	330.6	198
Water Solubility	insoluble	soluble	soluble
Density (g/cm^3)	1.2659	1.44	1.260

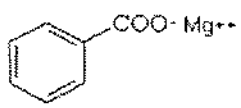
* Data for magnesium benzoate, potassium benzoate or calcium benzoate are expected to be similar to sodium benzoate.



Calcium Benzoate



Ammonium Benzoate



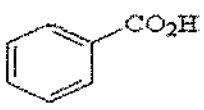
Benzoic Acid Mg++

IV. Hazard Assessment

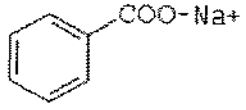
Table 3. Summary of Acute Toxicity Data on Benzoic Acid and Sodium Benzoate.

	Benzoic Acid			Sodium Benzoate		
Test	Species	Results	Category	Species	Results	Category
Oral LD_{50}	rat	2565 mg/kg	III	rat	3140 mg/kg	III
Dermal LD_{50}	rabbit	>2000 mg/kg	III		no data	
Inhalation LC_{50}	rat	>12.2 mg/l/4h.	IV		no data	
Eye Irritation	rabbit	severe irritation	I	rabbit	slightly irritating	III
Dermal Irritation	rabbit	non to slightly irritating	III	rabbit	non-irritating	IV
Dermal Sensitization	guinea pig	not sensitizing	Not applicable	human	nonimmunologic contact urticaria	Not applicable

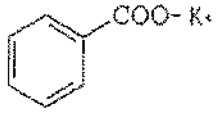
A. Toxicological Profile: The general effects of exposure to benzoic acid and sodium benzoate or its salts include nose and throat irritation if inhaled, as well as slight skin and severe eye irritation. Benzoic acid and the benzoate salts are rapidly metabolized and excreted, do not bioaccumulate, and have low toxicity after acute and repeated exposures. Early human consumption studies indicated no externally visible effects from ingesting 0.5 to 1.0 g/day of benzoic acid for 44 consecutive days or for 82/86 or 88/92 days (Gerlach 1909; as cited in USEPA IRIS). Assuming a human body weight of 70 kg, this corresponds to a dose of 14 mg/kg/day of benzoic acid. In another early study (1909), men who drank from 1 to 2.5 liters of apple juice containing 0.1 percent sodium benzoate complained of burning taste, headache, nausea and vomiting, itching of the skin, sweating, constipation and albuminuria. However, massive doses of sodium benzoate (25-60 g per day) were given to rheumatic patients without producing any harmful effects (FDA 1973). Adverse effects in humans given an oral



Benzoic Acid



Sodium Benzoate



Potassium Benzoate

bolus dose of less than or equal to 1.75 g/day of benzoic acid over a 20-day period include observed irritation, discomfort, weakness, and malaise (Wiley and Bigelow 1908; as cited in USEPA IRIS).

The oral LD_{50} for benzoic acid is 1,520 mg for the rabbit and 2,000 mg for the cat and dog. The lethal dose for benzoic acid in sheep is estimated to be 1,000 mg/kg (FDA 1973).

A chronic oral dose of 40 mg/kg/day of benzoic acid for 17 months was associated with decreased resistance to stress in mice and possibly with reduced food and water intake in rats after 18 months. However, another study reported by the same laboratory indicated 80 mg/kg/day in rats for 18 months was not associated with adverse effects on body weight, survival, or gross or microscopic pathology (Shtenberg and Ignat'er 1970; Ignat'er 1965; as cited in USEPA IRIS). Other long-term dietary studies showed decreased food intake and body weight in rats fed 1.5% benzoic acid (750 mg/kg/day). A reduced dose of 1.0% benzoic acid in the diet (50 mg/kg/day) did not produce signs of toxicity or adverse reproductive effects (Marquardt 1960; as cited in USEPA IRIS).

No positive results have been reported for benzoic acid or sodium benzoate when tested for mutagenicity or genotoxicity in prokaryotes, eukaryotes, and several mammalian test systems (McCann et al., 1975; Litton Bionetics, Inc., 1975 and 1975; Oikawa et al., 1980; as cited in USEPA IRIS).

B. Cations: Ammonium, Calcium, Magnesium, Potassium, and Sodium:

Calcium: The human body burden of calcium is approximately 1 kg for a 70 kg adult; thus, 1/70th of our weight is calcium. The calcium cation is necessary for bone and teeth formation. It is also important to the proper functioning of nerves, enzymes, and muscles, and plays a role in blood clotting and the maintenance of cell membranes. The recommended daily allowances (RDAs) for calcium are 1000 mg/day for adults aged 19 to 50 years, and 1200 mg/day for individuals older than 50 years.

Magnesium: The human body burden of magnesium is approximately 20 g for a 70 kg adult. The magnesium cation is also used in building bones. It plays a role in releasing energy from muscles and regulating body temperature. The RDA is 310 to 320 mg/day for adult females, and 400 to 420 mg/day for adult males, with the RDA increasing with increasing age.

Potassium: The human body burden of potassium is approximately 140 g for a 70 kg adult. The potassium cation is important in regulating blood pressure, regulating cellular water content, maintaining proper pH balance, and transmission of nerve impulses. It helps to regulate the electrical activity of the heart and muscles. The potassium RDA is 900 mg/day.

Sodium: The human body burden of sodium is approximately 20 g for a 70 kg adult. The sodium cation is necessary for the nerves and muscles to function properly. It is the principal cation of extracellular fluid, and helps to maintain the body's water balance. These electrolytes,

the electrically charged ions in the body fluids, consist to a great extent of sodium and potassium. There is no Recommended Daily Allowance (RDA) for sodium.

C. Ammonium Salt:

Ammonium salts dissociate to the negatively charged anion and the positively charged ammonium cation (NH_4^+). Humans cannot convert atmospheric nitrogen to any form that can be used as part of any of the various metabolic cycles. Therefore, reduced nitrogen (NH_4^+) has to enter the body from an outside source. These sources are the nitrogen-containing amino acids in protein which are consumed daily as part of the diet. Although the human body can produce some amino acids, ten amino acids are considered "essential" amino acids, i.e., they must be consumed in the diet.

Generally the body works to maintain a balance of nitrogen intake and nitrogen excretion. The estimated daily ammonia intake through food and drinking water is 18 mg. In contrast, 4000 mg of ammonia per day are produced endogenously in the human intestine.

Ammonia and the ammonium ion are integral components of normal human metabolic processes. Ammonia is released following deamination that occurs when protein is used by the body for energy production. The liver converts ammonia via the urea cycle into urea. According to FDA in the "Evaluation of the Health Aspects of Certain Ammonium Salts as Food Ingredients" (1974), "the normal liver so readily detoxifies ammonium ion from alimentary sources that blood concentrations of ammonium salts do not rise to the levels necessary to evoke toxic response." Approximately 80% of the body's excess nitrogen is eliminated through the kidneys as urea, approximately 25 to 30 grams per day.

D. Special Considerations for Infants and Children

Given the wide spread occurrence of benzoates in the food supply, the amount of benzoates that can be applied to food as a result of its use in a pesticide product should not significantly increase the existing amounts in the food supply. Oral doses of sodium benzoate appeared to have no maternal toxicity, fetal toxicity, or teratogenicity in mice, rats, hamsters, or rabbits with the highest doses tested being 175.0 mg/kg/day in mice and rats, 300.0 mg/kg/day in hamsters, and 250.0 mg/kg/day in rabbits (FDRL 1972; as cited in USEPA IRIS).

However, there is some concern that low birth weight or premature infants with immature livers can experience adverse effects when administered benzoic acid or benzoate salts. Infants with immature livers may not be capable of metabolizing benzoate. It was suggested that a combination of sodium benzoate and sodium phenylacetate not be administered to low birth weight infants unless the benefits outweigh the risks (AMA 1991; USP DI 1992, as cited in TOXNET).

EPA believes there would be a very low exposure of premature or very young infants to

benzoates. First, premature or very young infants ingest only formula or breast milk. (It is generally recommended that infants not consume solid food until 4 to 6 months of age.) Regulation of infant formulas is under the purview of the FDA. (www.fda.gov/fdac/features/596_baby.html) Benzoic acid and sodium benzoate are generally recognized as safe (GRAS) under 21 CFR 184.1021 and 184.1733, respectively. Therefore, infants consuming only infant formula or breast milk would be exposed to very low amounts of benzoates. Second, even if a young infant were to be fed some solid food, given the characteristics of benzoic acid and benzoate salts, residues are not likely to be present above naturally occurring concentrations. As discussed below (section 7) the benzoates are readily biodegradable. It is not likely to be taken up by plants.

Once past this several month time-period, there is no longer a concern for potential sensitivity to infants and children. Older infants, like adults, process benzoates through well understood metabolic pathways. A safety factor analysis has not been used to assess the risk. For the same reasons the additional tenfold safety factor is unnecessary.

V. Exposure Assessment

Benzoic acid and sodium benzoate have been used for decades in pharmaceuticals, cosmetics and/or in food as preservatives and flavoring/fragrance agents. According to information in Product Registers the substances are also used in different kinds of products, such as in paints, varnishes, solvents, cleaning and washing agents, photo chemicals, and antifreeze agents. Benzoic acid and sodium benzoate both have the status "generally recognized as safe" (GRAS) by the U.S. FDA. An estimated daily food input of benzoate by the U.S. EPA was 278 mg as sodium benzoate and 34 mg as benzoic acid. (USEPA 1987; as cited in USEPA IRIS). In 1983, the Joint Expert Committee on Food Additives (JEFCA) of the World Health Organization (WHO) established a group acceptable daily intake (ADI) for benzoic acid and its salt of 5 mg/kg body weight. This group ADI is based on the structural similarity and common metabolic fate of these chemicals (WHO 1997).

The National Research Council subcommittee also provided a possible daily human intake of benzoic acid and sodium benzoate in the total diet based on a comprehensive survey. The following table summarizes the possible daily intake for individuals in various age groups (FDA 1973).

Table 4. Possible daily intake

	Total Intake mg				mg/ kilogram of body weight*			
	Benzoic Acid		**Sodium Benzoate**		**Benzoic Acid**		**Sodium Benzoate**	
Age group	Avg.	Max.	Avg.	Max	Avg.	Max.	Avg.	Max.
0-5 mos.	0.6	1	10	21	.1	.2	2	4
6-11 mos.	6	21	111	313	.8	2.6	14	39
12-23 mos.	16	46	188	404	1.4	4.2	17	37

2-65+ yrs.	34	87	328	669	0.6	1.4	5.5	11

* Calculations based on an average weight of 60 kg for an adult and the following estimated weights of infants by age groups: 0-5 mos., 5 kg; 6-11 mos., 8 kg; and 12-23 mos., 11 kg.

It should also be noted that the NRC subcommittee stated the calculations of benzoate intakes are likely over stated, possibly by considerable margins. The Select Committee regarded the figures given in the table as levels that would unlikely be consumed by any of the age groups. Figures in the table were considered to be generous overestimates of the benzoic acid and sodium benzoate content of the human diet (FDA 1973).

The worldwide production capacity for benzoic acid is estimated at 700 kt. The major outlet (75% or 525 kt) for benzoic acid is for the production of phenol, which in turn is mainly used to produce caprolactam. The next biggest outlet is as a feedstock for sodium benzoate (10% or 70 kt) and chemical synthesis of plasticizers (5% or 35 kt). So, benzoic acid is mainly used in controlled industrial settings.

The worldwide production of sodium benzoate is estimated at 100 kt. The major use for sodium benzoate is as a preservative in food and beverages (60% or 60 kt). The second most important market for sodium benzoate is for cooling liquids (10% or 10 kt). Like sodium benzoate, potassium benzoate is used mainly as a preservative in nonalcoholic beverages with an estimated worldwide production capacity of only 7 kt. Ammonium benzoate is approved only as an indirect food additive for use only as component of adhesives (21 CFR 175.105). No production estimates could be determined for ammonium benzoate or any of the other benzoate salts.

The use of benzoic acid and sodium benzoate in pesticide products as inert ingredients is expected to result in much lower exposure than the FDA-regulated use of these compounds, as well as lower exposure than in the average daily intake of benzoates. Therefore, a quantitative screening-level exposure assessment has not been conducted.

VI. Risk Characterization

Benzoic acid is a naturally occurring compound found in berries and other foods. As previously discussed in this document, there are many FDA approved uses for benzoic acid and the benzoate salts. Residues from the pesticide uses of the benzoates are not likely to greatly contribute to the levels already approximated as the average daily intake.

As noted previously, three of the benzoates assessed in this document, benzoic acid, sodium benzoate, and ammonium benzoate, are included on the Agency's list of chemicals included in the High Production Volume (HPV) Challenge Program. HPV chemicals are those that are manufactured or imported into the United States in volumes greater than one million pounds per year. There are approximately 3,000 HPV chemicals that are produced or imported into the United States. The HPV Challenge Program is a voluntary partnership between industry, environmental groups, and the EPA which invites chemical manufacturers and importers to

provide basic hazard data on the HPV chemicals they produce/import. The goal of this program is to facilitate the public's right-to-know about the potential hazards of chemicals found in their environment, their homes, their workplace, and in consumer products. Based on the available toxicity data for the benzoates, the Agency feels confident in proceeding with this tolerance reassessment decision. Any submission of data by sponsors of benzoic acid, sodium benzoate, and ammonium benzoate as part of the HPV Challenge Program may, in the future, be used by OPP to revise or update their tolerance reassessment decision for these benzoates as deemed necessary and appropriate.

Taking into consideration all available information on benzoic acid, sodium benzoate, and the other salts of benzoate, including the FDA's designation of GRAS for benzoic acid and sodium benzoate, as preservatives/antimicrobial agents in foods and beverages, the historical use of benzoic acid and sodium benzoate in pharmaceuticals, cosmetics, as well as the natural presence of benzoic acid in berries, the use of ammonium benzoate as a preservative in adhesive components in foods, the use of benzoic acid and the benzoate salts as inert ingredients in pesticide formulations are unlikely to pose a significant hazard to the general public or any population subgroup. Therefore, HED is conducting a qualitative approach to assessing human health risks from exposure to benzoates.

VII. Environmental Fate/Ecotoxicity/Drinking Water Considerations:

The environmental fate and occurrence of benzoic acid has been well studied. The Hazardous Substances Database (HSDB) (www.toxnet.nlm.nih.gov) contains extensive summaries of the environmental fate of benzoic acid. In addition, HSDB information has been supplemented with predictive modeling based on structure activity relationships. For this analysis, sodium, potassium calcium, and magnesium salts were considered equivalent with respect to their environmental fate and ecotoxicity. Slight differences in physical-chemical properties were observed, but are not expected to impact their behavior or toxicity in the environment. Benzoic acid and the ammonium salt of benzoic acid were addressed separately.

Table 1 provides key fate and chemical properties for benzoic acid and representative molecules of the salts. With a pKa of 4.204, benzoic acid will dissociate to form an anion at environmental pH up to the limits of its solubility. The benzoate salts are highly water soluble and readily dissociate into the anion (benzoic acid) and cation (sodium, potassium, calcium, magnesium and ammonium ion). Thus, the environmental fate and effects of the benzoic acid salts are closely related to that of benzoic acid, and the free cation.

Table 1. Properties and Environmental Fate of Benzoic Acid and Selected Salts

Property	Benzoic Acid	Sodium Benzoate	Benzoic Acid, Ammonium Salt
Water Solubility (mg/L) @ 25C	3400 (M)	5.56E05 (M)	>1.0E06 (E)

Vapor Pressure mm Hg @ 25C	7E-04 (M)	3.67E-09 (E)	2.65E-07 (E)
Henry's Law Coefficient (atm-m^3/mole)	3.8E-08 (M)	1.09E-07 (E)	5.2E-16 (E)
Biodegradation	Primary: hours-days Ultimate: days-weeks	Primary: hours-days Ultimate: days-weeks	Primary: hours-days Ultimate: days-weeks
Log K_{ow}	1.87 (M)	-2.27 (E)	-1.33 (E)
K_{oc} (ml/g)	14 (E)	14 (E)	99
Hydrolysis Half-life @pH 7 (days)	No hydrolizable functional groups	No hydrolizable functional groups	52 days

M: Measured; E: Estimated

Based on low K_{oc}s and log K_{ow}s, benzoic acid and its salt are classified as highly mobile in soil (McCall). Volatilization from water would be minimal, based on both benzoic acid and the salts' low Henry's Law constant. All compounds have a low potential to volatilize from soil surfaces, based on vapor pressures of less than 1×10^{-4} mm Hg.

The biodegradability of benzoic acid has been extensively studied and are expected to be readily biodegradable in the environment. Using both unacclimated and acclimated sludge inoculums, benzoic acid degraded with half-lives of less than approximately 5 days. In most all cases, near complete mineralization occurred in under 10 days. In soil inoculums, benzoic acid exhibited a half-life for mineralization of 4.5 hours. In a second study, complete mineralization occurred in one day. Benzoic acid degraded in a polluted river water in 0.85 days and in reservoir water in 3.6 days. Degradation appears to be concentration dependent, with low concentrations, less than 1 ppb, mineralizing in eutrophic and oligotrophic lake water in under 7 days. Overall half-lives in unacclimated and acclimated systems ranges from hours to days for primary degradation and hours to weeks for ultimate (mineralization) degradation.

In an acidic soil, benzoic acid mineralized up to 80 percent in less than 12 weeks. The same experiment in a neutral soil resulted in approximately 70 percent mineralized in 12 weeks. Anaerobically, more than 75 percent of benzoic acid mineralizes when incubated for 8 weeks using sludge from a secondary digester. In several other experiments using sewage sludge inoculums, benzoic acid mineralized >90 percent in as little as 7 to 18 days. In a study using anoxic sediment from a hypereutrophic lake in Kalamazoo, MI, benzoic acid degraded completely (methane and CO_2) in one week.

Due to the lack of hydrolyzable functional groups, abiotic degradation of benzoic acid and the salts of benzoate would not be expected to be an important fate process. However, the ammonium salt would hydrolyze in neutral to alkaline environments from 5 days at pH 8 to 52 days at pH 7. Benzoic acid is expected to photolyze based on UV adsorption at 310nm. Available data indicate that 10.2 percent photolyzes in approximately 17 hours.

If any of these compounds were to enter the atmosphere, it is expected to exist solely as a vapor. Vapor-phase benzoic acid would be readily degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicles with an estimated half-life of 8 days.

Estimated toxicity (Meylan, 1998) indicates benzoic acid is the most toxic of the substances reviewed in this assessment. Table 2 lists the estimated toxicity for several species. Green algae and fish are among the most sensitive species based on predictive modeling for acute and chronic endpoints for all compounds. Based on the environmental fate profile of benzoic acid and its salts, exposures from labels uses are unlikely to reach concentrations necessary to elicit effects in aquatic organisms. Using laboratory rat data as a surrogate for terrestrial wild mammals and birds, benzoic acid and its salts do not appear to be very toxic and adverse effects from labeled uses is not expected.

Table 2. Ecotoxicity of Benzoic Acid and Selected Salts

Property	Benzoic Acid	Sodium Benzoate	Benzoic Acid, Ammonium Salt
Fish (96-h LC_{50}; mg/L)	1200	>1.0E06	1.4E05
Daphnid (48-h LC_{50}; mg/L)	1274	8.8E05	1.2E05
Green Algae (96-h EC_{50}; mg/L)	790	4.3E05	61172
Fish (30-day Chronic; mg/L)	151	71380	10486
Fish (SW) (96-h LC_{50}; mg/L)	258	32047	6374
Mysid Shrimp (96-h LC_{50}; mg/L)	380	>1.0E06	4.3E05
Green Algae (96-h Chronic; mg/L)	73	3646	893
Earthworm (14-day LC_{50}; mg/Kg dry wt.)	8238	18317	9081

Detections of benzoic acid in surface water have been extensively reported, but not quantified. In ground water, concentrations of <0.1 ppb have been reported for areas without known sources of potential contamination such as landfills, wood preserving facilities, and petroleum operations. Benzoic acid has been detected in the particulate fraction of rain and snow. In drinking water, concentrations of up to 15 ppm in the tap water of Otumwa, IA was reported, but was not detected in water from utilities in Seattle, Philadelphia, or Cincinnati. Benzoic acid has been detected, but not quantified, in other drinking water monitoring studies, domestically and internationally. Overall, and with few exceptions, concentrations of benzoic acid in ambient and drinking water is expected to be in the low ppb range.

VIII. Cumulative Exposure:

Section 408(b)(2)(D)(v) of the FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."

EPA does not have, at this time, available data to determine whether benzoic acid or the benzoate salts have a common mechanism of toxicity with other substances. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to benzoic acid or the benzoate salts and any other substances and benzoic acid or the benzoate salts do no appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that benzoic acid or the benzoate salts have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

References:

(Note to the Reader: MRID (Master Record Identification) Numbers were added to the references on October 17, 2003 and November 21, 2003. These numbers were not available at the time of document signature. No other changes were made to the document.)

AMA 1991. American Medical Association. AMA Drug Evaluations Annual 1991. Chicago, IL: American Medical Association, 1991. 2034

Anderson, F. Alan 2001. Forty-Fourth Report of the Cosmetic Ingredient Review Expert Panel. Final Report on the Safety Assessment of Benzyl Alcohol, Benzoic Acid, and Sodium Benzoate. (F. Alan Anderson). International Journal of Toxicology. Vol 20: Suppl 3: Pp 23-50. (MRID No. 46067601)

Department of Health and Human Services, National Institutes of Health, U.S. National Library of Medicine. Benzoic Acid; CAS Registry Number 65-85-0, Sodium Benzoate; CAS Registry Number 532-32-1, and Ammonium Benzoate; CAS Registry Number 1863-63-4. Available at http://www.toxnet.nlm.nih.gov.

FDA (Food and Drug Administration). 1973. Evaluation of the Health Aspects of Benzoic Acid and Sodium Benzoate as Food Ingredients. DHEW, Washington, DC. Report No. SCOGS-7. NTIS PB-223837/6. (MRID No. 46069301)

FDRL (Food and Drug Research Labs., Inc.). 1972. Teratologic Evaluation of FDA 71-37

(Sodium Benzoate). p.\75-79.

Gerlach, V. 1909. VII. Summary of the results. In: Physiological Activity of Benzoic Acid and Sodium Benzoate, V. Gerlach, Ed. Verlag von Heinrich Staadt, Wiesbaden. p.\90-92. (Cited in Informatics, Inc., 1972)

HSDB 2003. Hazardous Substances Database in http://www.toxnet.nlm.nih.gov

Ignat'ev, A.D. 1965. Experimental information contributing to a hygienic characterization of the combined effect produced by some food presentations. Vop. Pitan. 24(3): 61-68. (Cited in Informatics, Inc., 1972)

Litton Bionetics, Inc. 1974. Mutagenic Evaluation of Compound FDA 71-37, Sodium Benzoate. Report No. LBI 2446-297, FDA, Washington, DC, PB-245-453/6.

Litton Bionetics, Inc. 1975. Mutagenic Evaluation of Compound FDA 73-70, Benzoic Acid Certified A.C.S. Report No. LBI-2468-376; FDABF-GRAS-376 PB-245- 500/4.

McCall. McCall, P.J., D.A. Laskowski, R.L. Swann, H.J. Dishburger, "Measurements of Sorption Coefficients of Organic Chemicals on their use in Environmental Fate Analysis, Agricultural Products Department, Dow AgroChemicals USA, Midland, MI. P104 (89-109).

McCann, J., E. Choi, E. Yamasaki and B.N. Ames. 1975. Detection of carcinogens as mutagens in the Salmonella/microsome test: Assay of 300 chemicals. Proc. Natl. Acad. Sci. 72: 5135-5139.

Mylan, W. and P. Howard, 1998. ECOSAR Class Program, Version 0.99d. Syracuse Research Corporation, Syracuse, N.Y. For: U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, D.C.

Oikawa, A., H. Tohda, M. Kanai, M. Miwa and T. Sugimura. 1980. Inhibitors of poly(adenosine diphosphate ribose) induced sister chromatid exchanges. Biochem. Biophys. Res. Commun. 97(4): 1311-1316.

Shtenberg, A.J. and A.D. Ignat'ev. 1970. Toxicological evaluation of some combinations of food preservatives. Food Cosmet. Toxicol. 8(4): 369-380.

SIAR 2003. SIDS Initial Assessment Report. Benzoates Category. Pp1-34. (MRID 46107301, 46107501, 46107401, and 46107201)

USP DI 1992. US Pharmacopeia Dispensing Information; Drug Information for the Health Care

Professional 12th ed, V.I p. 2475.

U.S. EPA. 1987. Health and Environmental Effects Document for Benzoic Acid. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA IRIS 2003. U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on Benzoic Acid (65-85-0). Available from: http://www.epa.gov/ngispgm3/iris/index.html

WHO 1997. World Health Organization. Technical Report Series 868. Evaluation of Certain Food Additives and Contaminants. Forty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Geneva. (1997)

Wiley, H.M. and W.D. Bigelow. 1908. Influence of benzoic acid and benzoates on digestion and health. Bulletin 84, pt. IV, Bureau of Chemistry, U.S. Dept. Agriculture. (Cited in Informatics, Inc., 1972)

Fee for Service

This package includes the following	for Division
X New Registration	RD
Amendment	X AD
Waiver Request	BPPD
Voluntary Payment Request	

Receipt Nos. S- ~~82176-R~~ 771882

Product/Risk Manager: 31

EPA File Symbol/Reg. No. 82076-R

Pin-Punch Date: 12/16/04

Action Code:

Requested: A38

Granted: _____ Amount due: $90,000

VolPay Reduction:

____ % Original Decision #: D-

Parent/Child Decisions:

Reviewer: Mitchell Mitchell Date: 12.20.04

Remarks:

DP #: (313407)

PRIA

Decision #: 352089

DATA PACKAGE BEAN SHEET

Date: 17-Feb-2005

* * * Registration Information * * *

Registration: 82076-R - MICROL PRESERVATIVE

Company: 82076 - PETRO-CANADA

Risk Manager: RM 31 - Velma Noble - (703) 308-6233 Room# CM-2 308B

Risk Manager Reviewer: Tracy Lantz TLANTZ

Sent Date: 2/17/05 Calculated Due Date: 7/6/05 Edited Due Date:

Type of Registration: Product Registration - Section 3

Action Desc: (A38) NEW AI;FOOD USE;WITH EXEMPTION;

Ingredients: 009101, Benzoic acid(99.93%)

* * * Data Package Information * * *

Expedite: ● Yes ○ No Date Sent: 17-Feb-2005 Due Back:

DP Ingredient: 009101, Benzoic acid

DP Title: Product Chemistry

CSF Included: ● Yes ○ No Label Included: ● Yes ○ No Parent DP #:

Assigned To	Date In	Date Out
Organization: AD / PSB	2/18/05	
Team Name: CTT	2/18/05	
Reviewer Name: Bob T		
Contractor Name: DynCorp	2/22/05	6/10/05 gm

Administrative Due Date: 07-Feb-2007

Negotiated Due Date: 6/6/05

Projected Completion Date: 5/22/05

* * * Studies Sent for Review * * *

No Studies

* * * Additional Data Package for this Decision * * *

No Additional Data Packages

* * * Data Package Instructions * * *

Please Review the enclosed Product Chemistry Data:

Product ID, Comp. and Analysis - 464641-01
Physical and Chemical Properties - 464327-02

V- please copy beans / contra. (2 each)

1. DynCorp

2. Due 3/24/05

TY!

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES
Antimicrobials Division

June 16, 2005

SUBJECT: PRODUCT CHEMISTRY REVIEW OF: Micrel Preservative

DP Barcode: D313407 **Reg. No. Or File Symbol: 82076-R**
Manufacturing-use [ ] OR **End-use Product [X]**

TO: Velma Noble PM 31 / Tracy Lantz, Team Reviewer
Regulatory Management Branch I
Antimicrobials Division (7510C)

FROM: Robert A. Turpin, Chemist R. T.
Product Science Branch, CT Team
Antimicrobials Division (7510C)

THRU: Karen P. Hicks, CT Team Leader
Product Science Branch
Antimicrobials Division (7510C)

THRU: Michele E. Wingfield, Chief
Product Science Branch
Antimicrobials Division (7510C)

Product Formulation

Active Ingredient(s)	**% by wt.**
Benzoic acid	99.93

BACKGROUND: The applicant has submitted an application for registration of its product, benzoic acid, a preservative for food-grade lubricating oils. In support of the application the applicant has submitted a Confidential Statement of Formula (CSF), a draft product label, and studies containing data responding to the requirements of OPPTS Test Guidelines Series 830, Groups A&B.

Product ingredient source information may be entitled to confidential treatment

FINDINGS:

1. The CSF of the subject product is acceptable. The product is purchased from an unregistered source, [redacted] which certifies it to USP/FCC standards. Benzoic acid is a GRAS chemical.

2. MRID #464641-01: The report is a compilation of studies containing data responding to the requirements of OPPTS Test Guidelines Series 830, Group A - Product Identity, Composition, and Analysis. The data is acceptable.

3. MRID #464327-02: The report is a compilation of studies containing data responding to the requirements of OPPTS Test Guidelines Series 830, Group B - Physical and Chemical Properties. The data is acceptable.

RECOMMENDATIONS: None.

PRODUCT CHEMISTRY REVIEW

4. CONFIDENTIAL STATEMENT OF FORMULA

4a. Type of formulation and source registration

- Non-integrated formulation system [X]
  - Are all TGAIs used registered? Yes [ ] No [X]
- Integrated formulation system [ ]
- if "ME-TOO", specify EPA Reg. # of existing product:

4b. Clearance of inerts for non-food or food use:
Cleared for food use under 40 CFR §180.1001: Yes [X] No [ ] NA [ ]

4c. Physical state of product: Crystalline

4d. The chemical IDs and analytical information (including that for the TGAIs), density, pH, and flammability are consistent with that given in 830, Part B
Yes [X] No [ ]

4h. NCs and CLs are acceptable: Yes [X] No [ ] Not acceptable [ ]

4i. Active ingredient (s)	NC	LCL	UCL
Benzoic acid	99.93%	99.3%	100.0%

4j. For products produced by an integrated formulation system:

- All impurities of toxicological significance have a UCL?
  Yes [ ] No [ ] Not applicable [X]
- All impurities of $\geq 0.1\%$ in the product have been identified?
  Yes [ ] No [ ] Not applicable [X]

5. PRODUCT LABEL

5a. The active ingredients statement (chemical IDs and NC] is consistent with the CONFIDENTIAL STATEMENT OF FORMULA? Yes [X] No [ ]

5b. The formulation contains one of the following:

- 10% or more of a petroleum distillate: Yes [ ] No [X]
- 1.0% or more of methyl alcohol: Yes [ ] No [X]
- Sodium nitrite at any level: Yes [ ] No [X]
- a toxic List 1 inert at any level: Yes [ ] No [X]
- arsenic in any form: Yes [ ] No [X]

5c. If Yes to any of the above, does the inert ingredients statement contain a footnote indicating this? Yes [ ] No [ ] Not applicable [X]

5d. The appropriate warning statement regarding flammability or explosive characteristics of the product are listed on the label?
Yes [ ] No [ ] Not applicable [X]

5e. The storage and disposal instructions for the pesticide and container are in compliance with PR Notice 84-1 for household use products or PR Notice 83-3 for all other uses? Yes [X] No [ ] Not on label

5f. Does the product require an expiration date at which time the NC falls below the LCL (based on the one year storage stability data or other information)?
Yes [ ] No [X]

1. **PRODUCT CHEMISTRY (830 Series, Part A)**

Guideline	Acceptance of Information	MRID No.
830.1550[1] Product Identity	A	464641-01
830.1600 Description of Materials	A	464641-01
830.1620 Production Method[2]	A	464641-01
830.1650 Formulation process[3]	NA	
830.1670 Formation of impurities[4]	A	464641-01
830.1700 Preliminary Analysis[5]	A	464641-01
830.1750 Certified Limits[6]	A	464641-01
830.1800 Analytical Method[7]	A	464641-01

Explanation: A=acceptable; N=not acceptable; NA=technically not applicable; G=data gap; U=requires upgrading; W=waived; E=EPA estimate.

---

[1]See Confidential Appendix A for additional information

[2]For MP/EP products produced by an integrated formulation system.

[3]For products from a TGAI or MP.

[4]May be waived unless actual/possible impurities are of toxicological concern.

[5]Five batch analysis required for products produced by an integrated formulation system.

[6]If different from standard CIs recommended in 40 CFR 158.175, this should be discussed in Confidential Appendix A.

[7]Abbreviate method used as follows: gas chromatography (GC), infrared (IR), ultraviolet absorption (UV), nuclear magnetic resonance (NMR), etc.

6b. Physical/Chemical Properties*	Acceptance of data	Value or qualitative description	MRID No.
830.6302 Color	A	White	464327-02
830.6303 Physical state	A	Solid (crystalline powder)	464327-02
830.6303 Odor	A	Odorless-to-slight benzaldehyde	464327-02
830.7200 Melting point	A	122° C	464327-02
830.7220 Density/Relative density/bulk density	A	1.2659 @ 15° C	464327-02
830.7000 pH[1]	A	Saturated sol. @ 25° C = 2.8	464327-02
830.6314 Oxidation/Reduction	A	Contains no oxidizing/reducing agents. May react w/ oxidizers.	464327-02
830.6315 Flammability	NA	Flash point = 250° F	464327-02
830.6317 Storage stability	A	Stable	464327-02
830.7100 Viscosity	NA		
830.6319 Miscibility[2]	NA		
830.6320 Corrosion Character.	NA	Non-corrosive to polyethylene bags inside fiberboard drum.	464327-02
830.6321 Dielectric breakdown	NA	Not intended for use around electrical equipment	464327-02

Explanation: A=acceptable; N=not acceptable; NA=technically not applicable; G=data gap; U=requires upgrading; W=waived; E=EPA estimate.

* Provide brief description, e.g., color--yellow or property value, e.g., density 1.25 g/cc; Unless otherwise indicated, the property should be at 25 ^{0}C.

[1] If product is dispersible with water

[2] If product is an emulsifiable liquid

Tracy Lantz include in file for this product

PETRO-CANADA Lubricants

FAX

Petro-Canada Lubricants
2489 North Sheridan Way
Mississauga, Ontario, Canada L5K 1A8

Date: **June 16, 2005**
Number of pages including cover sheet: **5**

To: **Miss Karen Hicks**
Team Leader,
E.P.A. Anti-microbial Division
Fax: **703-308-6467**

From: **Inga Kuksis**
Specialty Products and Fluids, R&D
Phone: **905-804-4707**
Fax: **905-804-4740**

Dear Miss Hicks,

The following regards Petro-Canada's application for registration of MICROL (Reference # 82076-R).
Connie Welch of Chemreg has advised us that information regarding Good Laboratory Practices was requested for our application. We are having difficulties obtaining this kind of information, but have obtained an Iso 9001 Certificate issued to the manufacturer of the benzoic acid.
[redacted] does not manufacture the product as indicated by the attached letter.
We are continuing to pursue additional information, but hope that this may prove useful.

Inga Kuksis

Inga Kuksis
Specialty Products and Fluids
Petro-Canada Lubricants

Product ingredient source information may be entitled to confidential treatment

Pages 94 through 97 contains the identity of the source of product ingredients and is not included in this copy.

K592

TASK ASSIGNMENT FORM(TAF)

Antimicrobial Division/OPP--*Effective June 5, 1998*

PO: Bonaventure Akinlosotu

A -- Completed by Reviewer/Team Leader (*check(√) or complete appropriate boxes*)

RASSB___	PSB__X__	Product Toxicology	Human Toxicology	Product Chemistry X	Efficacy

Chemical: Benzoic acid | **Barcode:** D313407

Type: Registration_ RED_ Prod. Reregistration_ FQPA PRIA X Special Project_ Lit. Search_ Other_____

Due Date: ~~3/24/05~~ 4/8/05 **AD Contact:** Robert Turpin **Team Leader:** Karen Hicks

B -- Completed by Reviewer/Team Leader

Study/Action	MRID#	GDLN #	Gov't Est Hrs	**C - Completed By Contractor** Tech Hrs. Spent
MICROL Preservative Product Identity, Composition, and Analysis (Group A)	~~464327-01~~ 464641-01	830 Series	2	
MICROL Preservative Physical and Chemical Properties (Group B)	~~462173-02~~ 464327-02	830 Series	2	

Review Instructions/Comments

See attached page_

D -- Completed by WAM/PO

Action No: ~~K370~~ K592 | Date Sent: | WAM/PO: | Branch Chief (For Special Projects):

E -- Completed by Contractor

Date Delivered:	Delivery : Fed Ex_ Courier_ Electronic_ Other_
Principal Reviewers:	
Issues/Comments for Secondary Reviewer Attention: See attached page_	
F -- Completed by Secondary Reviewer(Antimicrobial Division)	
Minor Changes/Resolution with Contractor ___	Major Changes/Resolution with Contractor___
Secondary Review Hours___	Accepted ___ Unacceptable___
Reviewer Comments Recommendations: See attached page_	

DP #: (313407) Decision #: 352089

DATA PACKAGE BEAN SHEET

Date: 23-Feb-2005

* * * Registration Information * * *

Registration: 82076-R - MICROL PRESERVATIVE

Company: 82076 - PETRO-CANADA

Risk Manager: RM 31 - Velma Noble - (703) 308-8233 Room# CM-2 308B

Risk Manager Reviewer: Tracy Lantz TLANTZ

Sent Date: Calculated Due Date: Edited Due Date

Type of Registration: Product Registration - Section 3

Action Desc: (A38) NEW AI;FOOD USE;WITH EXEMPTION;

Ingredients: 009101, Benzoic acid(99.93%)

* * * Data Package Information * * *

Expedite: ● Yes ○ No Date Sent: 17-Feb-2005 Due Back:

DP Ingredient: 009101, Benzoic acid

DP Title: Product Chemistry

CSF Included: ● Yes ○ No Label Included: ● Yes ○ No Parent DP #:

	Assigned To	Date In	Date Out		
Organization:	AD / PSB	18-Feb-2005		Administrative Due Date:	07-Feb-2007
Team Name:	CTT	18-Feb-2005		Negotiated Due Date:	06-Jun-2005
Reviewer Name:	Middleton, Veronica			Projected Completion Date:	22-May-2005
Contractor Name:	DynCorp	23-Feb-2005			

* * * Studies Sent for Review * * *

No Studies

* * * Additional Data Package for this Decision * * *

No Additional Data Packages

* * * Data Package Instructions * * *

Please Review the enclosed Product Chemistry Data:

Product ID, Comp. and Analysis - 464641-01
Physical and Chemical Properties - 464327-02

Product ingredient source information may be entitled to confidential treatment

May 10, 2005

SUBJECT: PRODUCT CHEMISTRY REVIEW OF MICROL Preservative

DP Barcode: D313407 **Reg. No. Or File Symbol:** 82076-R
Manufacturing-use [ ] **End-use Product** [X]

TO: Wallace Powell, EPA Work Assignment Manager
FROM: John S. Chandler, CSS Work Assignment Manager

This is a review of the following Product Chemistry 830 Series study packages provided to CSC Systems & Solutions LLC (CSS) for preliminary review:

Product Identity, Composition and Analysis (Group A) (MRID 464641-01)

830 Series, Part A: 830.1550 (Product Identity and Composition), 830.1600 (Description of Materials Used to Produce the Product), 830.1620 (Description of Manufacturing Process), 830.1670 (Discussion of Formation of Impurities), 830.1700 (Preliminary Analysis), 830.1750 (Certified Limits), and 830.1800 (Enforcement Analytical Methods).

Physical and Chemical Properties (Group B) (MRID 464327-02)

830 Series, Part B: 830.6302 (Color), 830.6303 (Physical State), 830.6304 (Odor), 830.6313 (Stability to Normal and Elevated Temperatures, Metals and Metal Ions), 830.6314 (Oxidation/Reduction; Chemical Incompatibility), 830.6315 (Flammability/Flame Extension), 830.6316 (Explodability), 830.6317 (Storage Stability), 830.6319 (Miscibility), 830.6320 (Corrosion Characteristics), 830.6321 (Dielectric Breakdown Voltage), 830.7000 (pH), 830.7050 (UV/Vis Absorption), 830.7100 (Viscosity), 830.7200 (Melting Point/Melting Range), 830.7220 (Boiling Point/Boiling Range), 830.7300 (Density/Relative Density/Bulk Density), 830.7370 (Dissociation Constants in Water), 830.7550 (n-Octanol/Water Partition Coefficient), 830.7840 (Water Solubility), and 830.7950 (Vapor Pressure).

Product Formulation

Active Ingredients:	**% by wt.:**
Benzoic acid	99.93%

BACKGROUND:

On behalf of Petro-Canada, Specialty Products and Fluids (Petro-Canada), Chem Reg. International is submitting an application for registration of MICROL Preservative. MICROL Preservative is an food-use end-use product. Petro-Canada will be purchasing the food/USP-grade product from [redacted] (the manufacturer), re-label it in its original packaging and resell it

with antimicrobial claims. The end-use product contains the technical grade of the active ingredient (TGAI) and no additional ingredients. Benzoic acid (TGAI) is not currently an EPA registered product, and therefore the end-use product is produced by an integrated system. Benzoic acid is an inert list 4B product, and is not currently approved for food-contact uses under 40 CFR Part 180. The product, however, is in compliance with 21 CFR 178.3570 (lubricants with incidental food contact used on machinery used for producing, manufacturing, packaging, processing, preparing, treating, packaging, transporting, or holding food) at a maximum level of 1.0%). The product label directions instruct application to a maximum level of 1.0%. Additionally, the product is certified as USP/FCC grade, and meets the specifications in 21 CFR 184.1021, Food Chemicals Codex (FCC) and the United States Pharmacopeia/National Formulary.

FINDINGS:

Product Identity, Composition and Analysis (Group A) (MRID 464641-01)

- The certified limits provided on the Confidential Statement of Formula (CSF) (dated 11/22/04) do not agree with the standard certified limits. The active ingredient is an anhydrous form of the chemical, with water as an inert. The proposed upper and lower certified limits (UCL and LCL, respectively) for water, unlike those for benzoic acid (TGAI), are in agreement with the provided preliminary analysis, and agree with the manufacturer certificates of analysis. The LCL for the active ingredient should be 99.5%, and not as currently listed. The label ingredient statement, which lists the nominal concentration, is consistent with the CSF and conforms to recommendations of PR Notice 91-2.

- The following Part A product chemistry data requirements are complete: 830.1550 (Product Identity and Composition), 830.1600 (Description of Materials Used to Produce the Product), 830.1620 (Description of Manufacturing Process), 830.1670 (Discussion of Formation of Impurities), and 830.1800 (Enforcement Analytical Methods). 830.1750 (Certified Limits) will be complete once the LCL for benzoic acid (TGAI and MP) is corrected on the provided CSF.

- While the applicant has provided an otherwise complete 830.1700 (Preliminary Analysis) study, the applicant has claimed (p. 24) that the submitter of this study was neither the sponsor of this study nor conducted it, and does not know whether it has been conducted in accordance with 40 CFR Part 160. Preliminary analysis studies are subject to full GLP requirements as specified in 40 CFR Part 160. A similar statement (see next bullet point) has been provided for the rest of the studies (p. 3) included in this MRID.

- A Good Laboratory Practices (GLP) statement was included with this data package, stating that the report was not conducted in accordance with the requirements of 40 CFR Part 160, with the exception of the portion of the report which discusses the analysis of

representative batches. The latter part is in contradiction with the GLP statement given on p. 24 and discussed in the previous bullet point.

Physical and Chemical Properties (Group B) (MRID 464327-02)

- The applicant has justified not providing data for the following Part B product chemistry studies: 830.6316 (Explodability), 830.6319 (Miscibility), 830.6321 (Dielectric Breakdown Voltage), 830.7100 (Viscosity), and 830.7220 (Boiling Point/Boiling Range). The product does not contain any explosive ingredients, is not an emulsifiable liquid intended to be mixed with petroleum solvents, is not intended to be used around electrical equipment, and it is not a liquid.

- The applicant has not provided studies conducted in accordance with the 830 guidelines for the following studies submitted in this data package: 830.6302 (Color), 830.6303 (Physical State), 830.6304 (Odor), 830.6313 (Stability to Normal and Elevated Temperatures, Metals and Metal Ions), 830.6314 (Oxidation/Reduction; Chemical Incompatibility), 830.6315 (Flammability/Flame Extension), 830.6317 (Storage Stability), 830.6320 (Corrosion Characteristics), 830.7000 (pH), 830.7050 (UV/Vis Absorption), 830.7200 (Melting Point/Melting Range), 830.7300 (Density/Relative Density/Bulk Density), 830.7370 (Dissociation Constants in Water), 830.7550 (n-Octanol/Water Partition Coefficient), 830.7840 (Water Solubility), and 830.7950 (Vapor Pressure). The applicant has instead referenced data from Hazardous Substances Databank (HSDB) for benzoic acid (TGAI), and has included a copy of the database entry as an attachment to the study.

- All provisions of the GLP standards apply to the following product chemistry studies: 830.6313 (Stability to Normal and Elevated Temperatures, Metals and Metal Ions), 830.7550 (n-Octanol/Water Partition Coefficient), 830.7840 (Water Solubility: Column Elution Method), 830.7950 (Vapor Pressure), 830.6317 (Storage Stability). Data provided for these studies does not necessarily comply with the required GLP provisions.

- A GLP statement was included with the study package stating that the submitter of this study was neither the sponsor of the study nor conducted it, and does not know whether the study has been conducted in accordance with 40 CFR Part 160.

RECOMMENDATIONS:

We are not providing recommendations or acceptability statements.

PRODUCT CHEMISTRY REVIEW

4. CONFIDENTIAL STATEMENT OF FORMULA

4a. Type of formulation and source registration

- Non-integrated formulation system [ ]
  - Are all TGAIs used registered? Yes [ ] No [ ]
- Integrated formulation system [X]
- If "ME-TOO", specify EPA Reg. # of existing product:

4b. Clearance of inerts for non-food or food use:
Cleared for food use under 40 CFR §180.1001: Yes [ ] No [X] NA [ ]
See BACKGROUND

4c. Physical state of product: solid (powder)

4d. The chemical IDs and analytical information (including that for the TGAIs), density, pH, and flammability are consistent with that given in 830, Part B
Yes [X] No [ ]

4h. NCs and CLs are acceptable: Yes [ ] No [X] *See FINDINGS.*

4i. Active ingredient(s)	NC	LCL	UCL
A. Benzoic acid	99.93%	99.5%	100%

4j. For products produced by an integrated formulation system:

- All impurities of toxicological significance have a UCL?
  Yes [ ] No [ ] Not applicable [X]
- All impurities of $\geq 0.1\%$ in the product have been identified?
  Yes [ ] No [ ] Not applicable [X]

5. PRODUCT LABEL

5a. The active ingredients statement (chemical IDs and NC] is consistent with the CONFIDENTIAL STATEMENT OF FORMULA? Yes [X] No [ ]

5b. The formulation contains one of the following:

- 10% or more of a petroleum distillate: Yes [ ] No [X]
- 1.0% or more of methyl alcohol: Yes [ ] No [X]
- Sodium nitrite at any level: Yes [ ] No [X]
- a toxic List 1 inert at any level: Yes [ ] No [X]
- arsenic in any form: Yes [ ] No [X]

5e. If Yes to any of the above, does the inert ingredients statement contain a footnote indicating this? Yes [ ] No [ ] Not applicable [X]

5d. The appropriate warning statement regarding flammability or explosive characteristics of the product are listed on the label?
Yes [ ] No [ ] Not applicable [X]

5e. The storage and disposal instructions for the pesticide and container are in compliance with PR Notice 84-1 for household use products or PR Notice 83-3 for all other uses? Yes [X] No [ ]

5f. Does the product require an expiration date at which time the NC falls below the LCL (based on the one year storage stability data or other information)?
Yes [ ] No [ ] *Provided study is deficient (See FINDINGS).*

6. **PRODUCT CHEMISTRY (830 Series, Part A)**

6a. Data Requirements	Acceptance of Information	MRID No.
830.1550[1] Product Identity		464641-01
830.1600 Description of Materials		464641-01
830.1620 Production Method[2]		464641-01
830.1650 Formulation process[3]		464641-01
830.1670 Formation of impurities[4]		464641-01
830.1700 Preliminary Analysis[5]		464641-01
830.1750 Certified Limits[6]		464641-01
830.1800 Analytical Method[7] *Multiple USP Methods*		464641-01

Explanation: A=acceptable; N=not acceptable; NA=technically not applicable; G=data gap; U=requires upgrading; W=waived; E=EPA estimate.

[1]See Confidential Appendix A for additional information
[2]For MP/EP products produced by an integrated formulation system.
[3]For products from a TGAI or MP.
4May be waived unless actual/possible impurities are of toxicological concern.
[5]Five batch analysis required for products produced by an integrated formulation system.
[6]If different from standard CLs recommended in 40 CFR 158.175, this should be discussed in Confidential Appendix A.
[7]Abbreviate method used as follows: gas chromatography (GC), infrared (IR), etc.

Physical and Chemical Characteristics (Series 830, Part B)

6b. Physical/Chemical Properties*	Acceptance of data	Value or qualitative description	MRID No.
830.6302 Color		white powder	464327-02
830.6303 Physical State		solid (powder)	464327-02
830.6304 Odor		No noticeable odor or with a slight benzaldehyde-like odor. (Ref. HSDB 11/11/04).	464327-02
830.6313 Stability to Normal and Elevated Temperatures, Metals and Metal Ions		Stable but will sublime at 100°C. (Ref. HSDB 11/11/04).	464327-02
830.6314 Oxidation/Reduction; Chemical Incompatibility		Does not contain any oxidizing or reducing agents. However, as a weak acid, it may react with oxidizers. (Ref. HSDB 11/11/04).	464327-02
830.6315 Flammability/Flame Extension		NA. Product is not a liquid. Flash point 250°F by closed cup. (Ref. HSDB 11/11/04).	464327-02
830.6316 Explodability		NA. Does not contain any explodable components.	464327-02 NA
830.6317 Storage Stability		Stable. (Ref. HSDB 11/11/04).	464327-02
830.6319 Miscibility[2]		NA. Product is not an emulsifiable liquid intended to be mixed with petroleum solvents.	464327-02 NA
830.6320 Corrosion Characteristics		Does not react with packaging. (Ref. HSDB 11/11/04).	464327-02
830.6321 Dielectric Breakdown Voltage		NA. Product is not intended for use around electrical equipment.	464327-02 NA
830.7000 pH[1]		2.8 (saturated solution at 25°C). (Ref. HSDB 11/11/04).	464327-02

6b. Physical/Chemical Properties*	Acceptance of data	Value or qualitative description	MRID No.
830.7050 UV/Vis Absorption		Absorbs UV radiation up to approximately 310 nm, with a maximum at 252 nm. (Ref. HSDB 11/11/04).	464327-02
830.7100 Viscosity		NA. Product is not a liquid.	464327-02 NA
830.7200 Melting Point/Melting Range		122.4°C (Ref. HSDB 11/11/04).	464327-02
830.7220 Boiling Point/Boiling Range		NA. Product is not a liquid.	464327-02 NA
830.7300 Density/Relative Density/Bulk Density		Specific gravity is 1.2659 (at 15°C). (Ref. HSDB 11/11/04).	464327-02
830.7370 Dissociation Constants in Water		pKa is 4.19. (Ref. HSDB 11/11/04).	464327-02
830.7550 n-Octanol/Water Partition Coefficient		log Kow is 1.87. (Ref. HSDB 11/11/04).	464327-02
830.7840 Water Solubility		3.4×10^3 mg/L at 25°C. (Ref. HSDB 11/11/04).	464327-02
830.7950 Vapor Pressure		7×10^{-4} mm Hg at 25 °C. (Ref. HSDB 11/11/04).	464327-02

Explanation: A=acceptable; N=not acceptable; NA=technically not applicable; G=data gap; U=requires upgrading; W=waived; E=EPA estimate.

* Provide brief description, e.g., color--yellow or property value, e.g., density 1.25 g/cc; Unless otherwise indicated, the property should be at 25°C.

[1] If product is dispersible with water
[2] If product is an emulsifiable liquid

DP #: (315791) Decision #: 352089

DATA PACKAGE BEAN SHEET

Date: 12-May-2005

* * * Registration Information * * *

Registration: 82076-R - MICROL PRESERVATIVE

Company: 82076 - PETRO-CANADA

Risk Manager: RM 31 - Velma Noble - (703) 308-6233 Room# CM-2 308B

Risk Manager Reviewer: Tracy Lantz TLANTZ

Sent Date: 09-Feb-2005 Calculated Due Date: Edited Due Date:

Type of Registration: Product Registration - Section 3

Action Desc: (A38) NEW AI;FOOD USE;WITH EXEMPTION;

Ingredients: 009101, Benzoic acid(99.93%)

* * * Data Package Information * * *

Expedite: ○ Yes ● No Date Sent: 11-Apr-2005 Due Back:

DP Ingredient: 009101, Benzoic acid

DP Title:

CSF Included: ○ Yes ● No Label Included: ○ Yes ● No Parent DP #:

Assigned To		Date In	Date Out	
Organization:	AD / RASSB	11-Apr-2005	12-May-2005	Administrative Due Date: 01-Apr-2007
Team Name:	RASSB I	11-Apr-2005	12-May-2005	Negotiated Due Date:
Reviewer Name:	Quick, Bob	11-Apr-2005	05-May-2005	Projected Completion Date:
Contractor Name:				

* * * Studies Sent for Review * * *

No Studies

* * * Additional Data Package for this Decision * * *

Printed on Page 2

* * * Data Package Instructions * * *

Please have Bob Quick confirm the companies PPM calculations he has the information needed to do this.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

May 5, 2005

SUBJECT: Review of MICROL * Preservative Containing Benzoic Acid

FROM: Robert Quick, Chemist
Risk Assessment and Science Support Branch
Antimicrobials Division(7510C)

TO: Velma Noble, Product Manager Team 31
Regulatory Management Branch I
Antimicrobials Division(7510C)

THRU: Norm Cook, Chief
Risk Assessment and Science Support Branch
Antimicrobials Division(7510C)

ID#: 82076-R - MICROL PRESERVATIVE

DP BARCODE: D315791

DECISION: 352089

PC CODE: 009101

CHEMICAL NAME: Benzoic Acid

MRID#: None

Background:

Chem Reg International has submitted this registration action to the Agency on behalf of Petro-Canada Lubricants Division.

The proposed use is to add benzoic acid as a material preservative to mineral oil that can be used as a component of lubricating oils that have incidental food contact when used on machinery used for producing, manufacturing, packing, processing, preparing, treating, packaging, transporting or holding food. Benzoic acid will be permitted in mineral oil at a level of 1%.

Benzoic acid has clearances for both the Food & drug Administration(FDA) and with the EPA. Benzoic acid is cleared by the FDA as GRAS as a direct food substance(21 CFR 184.1021) and is permitted at a level of 0.1% in food(0.1% is equivalent to 1,000 ppm).

Mineral oil has an FDA clearance in food processing equipment at a level not to exceed 10 ppm in food(21 CFR 178.3570).

Personal communication with Ms Tracy Lantz, PM Team 31 confirms that a complete review of this proposed use is not needed. The registrant states that the benzoic acid level from the proposed use, assuming 100% transfer of residue to food, would be 0.05 ppm. Ms Lantz wants RASSB to confirm the registrant's calculation.

The "bean sheet", D315791, bears the instructions, "Please have Bob Quick confirm the companies PPM calculations he has the information needed to do this".

RASSB Calculation

Proposed level of benzoic acid in mineral oil: 1.0%
Mineral oil level permitted in lubricating oil for food contact: 10 ppm

Assuming all benzoic acid in the mineral migrates to the food. Then:

0.01(% of benzoic acid in mineral oil) x 10 ppm(level of mineral oil permitted in lubricating oil applied to food machinery)

is

0.01 x 10 ppm = 0.1 ppm benzoic acid in food

This level is far less than the 1,000 ppm of benzoic acid level that is already permitted in food as a direct food substance by the FDA(21 CFR 184.1021).

Note: An earlier benzoic acid residue value of 0.05 ppm in food cited by the registrant was

taken from a then proposed use pattern which was for 0.5 % benzoic acid in mineral oil (the level of benzoic acid in mineral oil is now proposed at 1%).

meeting minutes sent to Velma/ Dennis on 9/22/05

MINUTES

Benzoic Acid Scoping Meeting
New AI with Food Use
3/30/05 4:00-5:00 PM

9/25/05 Dennis said these minutes were good.

Attendees: Frank Sanders, Jack Housenger, Norm Cook, Dennis Edwards, Bob Quick, Debbie Smegal, Wallace Powell, Velma Noble, Karen Hicks, Tracy Lantz

Purpose of Meeting:
To determine if any additional reviews, other than chemistry are required to register this new active ingredient. Do we need a RASSB or Tox review?

Background:

Petro-Canada has applied to register this product/new A.I..
$90,000 paid, start date is 1/6/05.
This is an A38 **New AI, Food Use**, with Exemption.
Would like to add USP benzoic acid (>99% purity) to the mineral oil component of lubricants.
State that they will comply with 21 CFR 178.3570 (a) (1) with incidental food contact use on machinery used for producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food.
They would like to add the benzoic acid at a maximum level of 1.0% to prevent decomposition and odors in the lubricant caused by microorganisms.
Petro-Canada states that the highest level of contact with food is: 0.10 ppm

AI has been registered in the past, but no current registrations
Benzoic Acid is listed in 21 CFR Part 184 (B) as GRAS
It is described in 21 CFR 184.1021 as occuring in nature in foods such as cranberries, prunes, plums, cinnamon, ripe cloves, and most berries.

Regulated by the FDA as a food additive (21 CFR 184.1021 (d) @ 0.1% in food.)

Using a unregistered source of AI

Toxicology: company states that sodium benzoate is rapidly metabolized to benzoic acid in mammals. Benzoic acid itself is rapidly metabolized in the liver by conguation with glycine, resulting in formation of hippuric acid, which then is rapidly excreted via the urine. Toxicological data on sodium benzoate can be used to support benzoic acid.

Discussion and Conclusions:

Karen's group is already doing a chemistry review.

Debbie discussed the fact that HED had already done two reviews on sodium benzoate, one completed in 2003 showed no tox endpoints and that it has also been characterized by HED as low risk.

Does RASSB need to do an assessment? NO

But we will ask Bob Quick to confirm in writing the highest level of Benzoic acid in contact with food. Bob thinks that it is 0.10 ppm which falls within our standards, but he will confirm this. We will use a BEAN to request this information from Bob.

Do we need a Tox assessment? (From PSB)

Karen suggested that we do send a BEAN to PSB so that they can give input as to whether they feel the tox language on the label is appropriate. They will do their review based on the documents referred to by Debbie on Sodium Benzoate.

Debbie provided e-copies of the two reviews to which she had referred.

attendees Bob Quick Frank Sanders
Dennis Edwards Debbie Smegal Tracy
Jacki Housenger Norm Cook Wallace Powell

Benzoic Acid Scoping Meeting
New AI with Food Use
3/23/05 11:00 AM-12:00 PM

Velma Noble
Karen Hicks
Tracy Lantz

Rescheduled:
3/30/05 4:00-5:00 PM

follow up this meeting as a memo → then email to all for any additional comments

Summary

Karen is already doing chemistry

Velma + Tracy spoke on 4/5/05 She will send Bean to Bob Q and Karen (for Tox) of HED reviews

Purpose of Meeting:
To determine if any additional reviews, other than chemistry are required to register this product. Do we need a RASSB or Tox review?

Tox I for eye

Background:

only register 99% product

Petro-Canada has applied to register this product.
✓$90,000 paid, start date is 1/6/05.
✓This is an A38 **New AI, Food Use**, with Exemption.
✓**Would like to add USP benzoic acid (>99% purity) to the mineral oil component of lubricants.**
State that they will comply with 21 CFR 178.3570 (a) (1) with incidental food contact use on machinery used for producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food.
They would like to add the benzoic acid at a maximum level of 1.0% to prevent decomposition and odors in the lubricant caused by microorganisms.
Petro-Canada states that the highest level of contact with food is: ~~0.05 ppm~~ → 0.10 ppm
(This number doesn't make sense, does Bob Quick agree with this calculation?)

mineral oil is 10 ppm in oil if add

0.10 ppm within the standards as per Bob Quick

AI has been registered in the past, but no current registrations
Benzoic Acid is listed in 21 CFR Part 184 (B) as GRAS
It is described in 21 CFR 184.1021 as occuring in nature in foods such as cranberries, prunes, plums, cinnamon, ripe cloves, and most berries.
It may be used as a antimicrobial agent as defined in 170.3 (o)(2) (substances used to preserve food by preventing growth of microorganisms and subsequent spoilage) and as a flavoring agent and adjunct as defined in 170.3 (o)(12).

two risk assessments follow

Debbie Smegal | HED review from 2003 - there are no endpoints ← HED Low risk document has characterized benzoic acid. Also characterized acids

Sodium benzoate converts to benzoic acid under acidic conditions. Data on both compounds is relevant. Benzoic acid is currently regulated as a list 4B inert with exemptions from the requirements for a tolerance as an inert (and occasionally active) ingredient in pesticide formulations under 40 CFR 910 as an inert preservative.

Regulated by the FDA as a food additive (21 CFR 184.1021 (d) @ 0.1% in food.)

Using a unregistered source of AI
Submitted 2 different data matrixes, one with MRID's the other without

Toxicology: company states that sodium benzoate is rapidly metabolized to benzoic acid in mammals. Benzoic acid itself is rapidly metabolized in the liver by conguation with glycine, resulting in formation of hippuric acid, which then is rapidly excreted via the urine. Toxicological data on sodium benzoate can be used to support benzoic acid. (But does this explanation just support the oral route of exposure or all routes?)

Conclusion:

Does RASSB need to do an assessment? No

If so what review? None

Give Bob Quick a Bean for him to confirm the level of Benzoic acid in context of food
sent 4/1/05

Environmental? No

Do we need a Tox assessment? (From PSB) — Wallace

Karen agrees of labeling
Karen's group should do a review based on sodium benzoate.

Give Karen a Bean > May due date.
sent 4/1/05

Velma will do this
↓
refer to HED Low Risk [illegible] — maybe doesn't need to go to

Get copy of HED review from Debbie Smegal

if need an actual review [illegible] Karen

Velma

Benzoic Acid Scoping Meeting
New AI with Food Use
3/23/05 11:00 AM-12:00 PM

Rescheduled:
3/30/05 4:00-5:00 PM

Summary

Purpose of Meeting:
To determine if any additional reviews, other than chemistry are required to register this product. Do we need a RASSB or Tox review?

Background:

Petro-Canada has applied to register this product.
$90,000 paid, start date is 1/6/05.
This is an A38 **New AI, Food Use**, with Exemption.
Would like to add USP benzoic acid (>99% purity) to the mineral oil component of lubricants.
State that they will comply with 21 CFR 178.3570 (a) (1) with incidental food contact use on machinery used for producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food.
They would like to add the benzoic acid at a maximum level of 1.0% to prevent decomposition and odors in the lubricant caused by microorganisms.
Petro-Canada states that the highest level of contact with food is: 0.05 ppm
(This number doesn't make sense, does Bob Quick agree with this calculation?)

AI has been registered in the past, but no current registrations
Benzoic Acid is listed in 21 CFR Part 184 (B) as GRAS
It is described in 21 CFR 184.1021 as occuring in nature in foods such as cranberries, prunes, plums, cinnamon, ripe cloves, and most berries.
It may be used as a antimicrobial agent as defined in 170.3 (o)(2) (substances used to preserve food by preventing growth of microorganisms and subsequent spoilage) and as a flavoring agent and adjunct as defined in 170.3 (o)(12).

Sodium benzoate converts to benzoic acid under acidic conditions. Data on both compounds is relevant. Benzoic acid is currently regulated as a list 4B inert with exemptions from the requirements for a tolerance as an inert (and occasionally active) ingredient in pesticide formulations under 40 CFR 910 as an inert preservative.
Regulated by the FDA as a food additive (21 CFR 184.1021 (d) @ 0.1% in food.)

Using a unregistered source of AI
Submitted 2 different data matrixes, one with MRID's the other without

Toxicology: company states that sodium benzoate is rapidly metabolized to benzoic acid in mammals. Benzoic acid itself is rapidly metabolized in the liver by conguation with glycine, resulting in formation of hippuric acid, which then is rapidly excreted via the urine. Toxicological data on sodium benzoate can be used to support benzoic acid. (But does this explanation just support the oral route of exposure or all routes?)

Conclusion:

Does RASSB need to do an assessment?

If so what review?

Environmental?

Do we need a Tox assessment? (From PSB)

Benzoic Acid Scoping Meeting
New AI with Food Use
~~3/23/05~~ 11:00 AM-12:00 PM
3/30/05 4:00 – 5:00 PM

Attendees

Bob Quick, RASSB
Dennis Edwards RMB1
Frank Sanders
Jack Housenick
Wallace Powell
Norm Cook
Debbie Smegal
Karen Hicks
Tracy L
Velma N.

Calendar Entry

☐ Notify me ☐ Mark Private ☐ Pencil In

Subject	Scoping Meeting on Benzoci Acid Rescheduled New AI Food Use
When	Starts Wed 03/30/2005 04:00 PM; Ends Wed 03/30/2005 05:00 PM; 1 hour; ☐ Specify a different time zone
Invitees	Required (to): Dennis Edwards/DC/USEPA/US@EPA, Frank Sanders/DC/USEPA/US@EPA, Jack Housenger/DC/USEPA/US@EPA, Karen; Optional (cc): ; FYI (bcc):
Chair	Tracy Lantz/DC/USEPA/US
Where	Location: ; Rooms: ; Resources: 308u; Online: ☐ This is an Online
Categorize	

Scheduler — Move the time bar to change the time and duration of the meeting. When the time bar is green, all required and optional can attend.

Show ☐ Summary ● Details

Thursday, March 31, 2005

Invitees	2 pm	3 pm	4 pm	7 am	8 am	9 am	10 am	11 am	12 pm	1 pm	2 pm
Dennis Edwards/DC/USEPA											
Frank Sanders/DC/USEPA/U											
Jack Housenger/DC/USEPA											
Karen Hicks/DC/USEPA/US											
Michele Wingfield/DC/USEP											
Norm Cook/DC/USEPA/US											
Rachel McCrea/DC/USEPA/											
Velma Noble/DC/USEPA/US											
Scheduled Rooms											
Scheduled Resources											
308u											

Available ▒ Already Scheduled ▒ Unavailable ▒ No info ▒ Info Restricted

Description

<Enter the description of this event>

Dennis Edwards
Frank, Jack
Michele W.
Norm Velma

Calendar Entry

☐ Notify me ☐ Mark Private ☐ Pencil In

Subject	Scoping Meeting on Benzoic Acid-New AI Food Use-from Petro-Canada
When	Starts Wed 03/23/2005 11:00 AM; Ends Wed 03/23/2005 12:00 PM; 1 hour; ☐ Specify a different time zone
Invitees	Required (to): Frank Sanders/DC/USEPA/US@EPA, Jack Housenger/DC/USEPA/US@EPA, Dennis Edwards/DC/USEPA/US@EPA, Velma; Optional (cc): ; FYI (bcc):
Chair	Tracy Lantz/DC/USEPA/US
Where	Location: Room 308 U; Rooms: ; Resources: ; Online: ☐ This is an Online
Categorize	

Scheduler — Move the time bar to change the time and duration of the meeting. When the time bar is green, all required and optional can attend.

Show ○ Summary ● Details

Wednesday, M ▾ :h 2

Invitees	9 am	10 am	11 am	12 pm	1 pm	2 pm	3 pm	4 pm	5 pm	6 pm	7 pm
Tracy Lantz/DC/USEPA/US											
Required											
Dennis Edwards/DC/USEPA											
Frank Sanders/DC/USEPA/I											
Jack Housenger/DC/USEPA											
Michele Wingfield/DC/USEF											
Norm Cook/DC/USEPA/US											
Rachel McCrea/DC/USEPA/											
Scheduled Rooms	9 am	10 am	11 am	12 pm	1 pm	2 pm	3 pm	4 pm	5 pm	6 pm	7 pm
Karen Hicks											
Velma Noble											
Scheduled Resources	9 am	10 am	11 am	12 pm	1 pm	2 pm	3 pm	4 pm	5 pm	6 pm	7 pm

Available ▒ Already Scheduled ▒ Unavailable ▒ No Info ▒ Info Restricted

Description

The purpose of this meeting is to determine if any additional reviews, other than chemistry will be required.
I will distribute background materials prior to the meeting. This AI has already been cleared under 21 CFR as a food additive.
Michele, please invite a toxicologist to this meeting. I have sent the chemistry data for review.

Connie B. Welch

From: Connie B. Welch
Sent: Tuesday, March 22, 2005 9:58 AM
To: 'noble.velma@epa.gov'

Velma,
Thanks for the discussion this morning! As for the corrections, I only found one page that did not get corrected. In the Group A report it is correct. It is the introductory paragraph which states "The intended use pattern as an antimicrobial active ingredient is indoor, nonfood, as a material preservative for use in the mineral oil component of lubricants compliant with 21 CFR 178.3570 (lubricants with incidental food contact used on machinery used for producing, manufacturing , packing, processing, preparing, treating, packaging, transporting, or holding food) at a maximum level of 1.0%, in order to prevent decomposition and odors in the lubricant caused by microorganisms".

I have reviewed the submission to EPA and the only other place I have found this introductory paragraph where the .5% was not corrected (should be 1.0% as stated above) is in the ecotox submission for the 850.1010 and 850.1075 guideline requirements. It contains the same introductory paragraph, but it has a maximum level of .5%. It should be corrected to read "maximum level of 1.0 %" as stated above.

I will fax in a corrected page. Thanks again for your help. I look forward to hearing of the good outcome!

--Connie

Connie B. Welch
Global Regulatory Consultant
ChemReg International, LLC
1990 Old Bridge Road, Suite 201
Lake Ridge, VA 22192

Phone: 703-492-7905
Fax: 703-492-0668
Email: welch@chemreg.com

ChemReg International, LLC

1990 Old Bridge Road, Suite 201
Lake Ridge, Virginia 22192-2383

Phone: 703-492-0445
Fax: 703-492-0668

Web Sites: www.chemreg.com
www.pesticide.net

Tox info. does this need to go to [illegible]?

Benzoic Acid

FAX MESSAGE

DATE: March 22, 2005

TO: Ms. Velma Noble **FAX:** 703-308-6466

FROM: Ms. Connie Welch

PAGES: 7

MESSAGE:

Velma,
I thought I would resend the entire package with the corrected page. It may be easier to hand off to RASSB the entire corrected package (even if the correction is minor). Thanks again for all of your help.

ChemReg
INTERNATIONAL, LLC

1990 OLD BRIDGE ROAD, SUITE 201
LAKE RIDGE, VIRGINIA 22192-2383

PHONE: 703-492-0445
FAX: 703-492-0668

WEB SITES: www.chemreg.com
www.pesticide.net

FAX MESSAGE

DATE: March 22, 2005

TO: Ms. Velma Noble **FAX:** 703-308-6466

FROM: Ms. Connie Welch

PAGES: 4

MESSAGE:

Velma,
Thanks so much! I am attaching a corrected page as per my email. Take care!

Study Title

MICROL Preservative
Ecotoxicology

Data Requirement

US-EPA Guideline Number OPPTS Series 850

850.1010 Aquatic Invertebrate Acute Toxicity
850.1075 Fish Acute Toxicity

Author

E. A. Brown
ChemReg International, LLC
1990 Old Bridge Road, Suite 201
Lake Ridge, VA 20192

Sponsor

Petro-Canada
Specialty Products and Fluids
2489 North Sheridan Way
Mississauga, Ontario Canada L5K 1A8

Study Completion Date

December 2, 2004

Report Number

MICROL-2004-04

Total pages: 52

Statement of Data Confidentiality Claim

No information is claimed confidential on the basis of its falling within the scope of FIFRA § 10(d)(1)(A), (B), or (C).

Company: Petro-Canada
Specialty Products and Fluids

Submitter Name: Elizabeth Anne Brown
ChemReg International, LLC
Authorized Agent for Petro-Canada

Signed: Elizabeth Anne Brown

Date: December 2, 2004

Study Title

MICROL Preservative
Ecotoxicology

Data Requirement

US-EPA Guideline Number OPPTS Series 850

850.1010 Aquatic Invertebrate Acute Toxicity
850.1075 Fish Acute Toxicity

Author

E. A. Brown
ChemReg International, LLC
1990 Old Bridge Road, Suite 201
Lake Ridge, VA 20192

Sponsor

Petro-Canada
Specialty Products and Fluids
2489 North Sheridan Way
Mississauga, Ontario Canada L5K 1A8

Study Completion Date

December 2, 2004

Report Number

MICROL-2004-04

Total pages: 52

INTRODUCTION

MICROL PRESERVATIVE is 100% of USP (food) grade benzoic acid. The intended use pattern as an antimicrobial active ingredient is ***Indoor, nonfood***, as a material preservative for use in the mineral oil component of lubricants compliant with 21 CFR 178.3570 (lubricants with incidental food contact used on machinery used for producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food) at a maximum level of 1.0 %, in order to prevent decomposition and odors in the lubricant caused by microorganisms.

Benzoic Acid (CAS RN 65-85-0) is an extremely well known, widely-studied, and widely used compound, particularly as a preservative for food (direct food additive). The closely related and equally well known, widely-studied, and widely used compound, sodium benzoate (CAS RN 532-32-1) converts to benzoic acid under acid conditions. Data on both compounds can be considered as relevant. Benzoic acid occurs naturally, while sodium benzoate does not. The antimicrobial activity of both compounds is from benzoic acid. Both compounds are widely approved on an international basis as direct food additives. Both compounds are widely used a preservatives in other applications (such as in cosmetics). Benzoic acid is endogenous in the human body.

There is adequate information in the public literature to address the required data requirements. The public literature is discussed below.

OPPTS 850 AQUATIC INVERTEBRATE ACUTE TOXICITY

For the toxicity data mentioned, it is not always stated whether the cited effect values are based on nominal or measured concentrations of benzoic acid or sodium benzoate. However, because of their water solubility, their insignificant volatility, and their low adsorption potential, all nominal concentrations of the test substances are expected to correspond to effective concentrations, even in tests with open systems and longer exposure durations.

As benzoic acid itself is only slightly soluble in water, sodium benzoate -- which, under acidic conditions, converts to undissociated benzoic acid, often is used in place of benzoic acid.

The 24hr EC50 of benzoic acid to Daphnia magna is 500 mg/L (Bringmann & Kuehn 1982, as cited by WHO 2000)

"Ninety-six-hour LC_{50} values of >100 mg sodium benzoate/litre have been found for *Daphnia magna* (first and second larval instar) and *Gammarus fasciatus* (juvenile: 7 mg in size) under static test conditions (multispecies test; pH 6.5-8; 20°C) (Ewell et al., 1986). The same was true for juveniles of other invertebrates tested simultaneously: *Asellus intermedius* (Arthropoda; 12 mg body weight), *Dugesia tigrina* (Platyhelminthes; 6 mg body weight), *Helisoma* trivolvis (Mollusca; 180 mg body weight), and *Lumbriculus variegatus* (Annelida; 6 mg body weight) (Ewell et al., 1986)." (WHO 2000)

OPPTS 850.1075 ACUTE TOXICITY TO FISH

"Two different tests with the freshwater fathead minnow *(P. promelas*; juvenile stages) resulted in 96-h LC_{50} values of 484 mg sodium benzoate/litre (measured concentration; flow-through system; pH 7.4; 24°C) (Geiger et al., 1985) and >100 mg/litre (nominal concentration; static system; pH 6.5-8.5; 20°C) (Ewell et al., 1986)." (WHO 2000)

Good Laboratory Practices Statement

The submitter of this study was neither the sponsor of this study nor conducted it, and does not know whether it has been conducted in accordance with 40 CFR Part 160.

Author
Submitter: Elizabeth Anne Brown Date: Dec 2, 2004

Elizabeth Anne Brown
ChemReg International, LLC

Table of Contents

INTRODUCTION

MICROL PRESERVATIVE is 100% of USP (food) grade benzoic acid. The intended use pattern as an antimicrobial active ingredient is ***Indoor, nonfood***, as a material preservative for use in the mineral oil component of lubricants compliant with 21 CFR 178.3570 (lubricants with incidental food contact used on machinery used for producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food) at a maximum level of 1.0 %, in order to prevent decomposition and odors in the lubricant caused by microorganisms.

Benzoic Acid (CAS RN 65-85-0) is an extremely well known, widely-studied, and widely used compound, particularly as a preservative for food (direct food additive). The closely related and equally well known, widely-studied, and widely used compound, sodium benzoate (CAS RN 532-32-1) converts to benzoic acid under acid conditions. Data on both compounds can be considered as relevant. Benzoic acid occurs naturally, while sodium benzoate does not. The antimicrobial activity of both compounds is from benzoic acid. Both compounds are widely approved on an international basis as direct food additives. Both compounds are widely used a preservatives in other applications (such as in cosmetics). Benzoic acid is endogenous in the human body.

There is adequate information in the public literature to address the required data requirements. The public literature is discussed below.

OPPTS 850 AQUATIC INVERTEBRATE ACUTE TOXICITY

For the toxicity data mentioned, it is not always stated whether the cited effect values are based on nominal or measured concentrations of benzoic acid or sodium benzoate. However, because of their water solubility, their insignificant volatility, and their low adsorption potential, all nominal concentrations of the test substances are expected to correspond to effective concentrations, even in tests with open systems and longer exposure durations.

As benzoic acid itself is only slightly soluble in water, sodium benzoate -- which, under acidic conditions, converts to undissociated benzoic acid, often is used in place of benzoic acid.

The 24hr EC50 of benzoic acid to Daphnia magna is 500 mg/L (Bringmann & Kuehn 1982, as cited by WHO 2000)

"Ninety-six-hour LC_{50} values of >100 mg sodium benzoate/litre have been found for *Daphnia magna* (first and second larval instar) and *Gammarus fasciatus* (juvenile: 7 mg in size) under static test conditions (multispecies test; pH 6.5-8; 20°C) (Ewell et al., 1986). The same was true for juveniles of other invertebrates tested simultaneously: *Asellus intermedius* (Arthropoda; 12 mg body weight), *Dugesia tigrina* (Platyhelminthes; 6 mg body weight), *Helisoma* trivolvis (Mollusca; 180 mg body weight), and *Lumbriculus variegatus* (Annelida; 6 mg body weight) (Ewell et al., 1986)." (WHO 2000)

OPPTS 850.1075 ACUTE TOXICITY TO FISH

"Two different tests with the freshwater fathead minnow *(P. promelas*; juvenile stages) resulted in 96-h LC_{50} values of 484 mg sodium benzoate/litre (measured concentration; flow-through system; pH 7.4; 24°C) (Geiger et al., 1985) and >100 mg/litre (nominal concentration; static system; pH 6.5-8.5; 20°C) (Ewell et al., 1986)." (WHO 2000)

APPENDIX
WHO. 2000. CONCISE INTERNATIONAL CHEMICAL ASSESSMENT DOCUMENT NO. 26. BENZOIC ACID AND SODIUM BENZOATE.

March 2, 2005

Tracy's
read thru - need
to summarize
for presentation
@ meeting.

Subject: Scoping Meeting for Benzoic Acid
New AI, Food Use
Submitted by Petro Canada

Meeting: 3/23/05
11:00-12:00
Room 308U

Dear Frank, Jack, Dennis, Michele, Norm, and Velma,

Just some background information to assist in our scoping meeting including: several letters from the company, CSF, label, 2 sets of data matrixes, and my informal notes on this submission.

Basically, Petro Canada would like to add Benzoic acid to the mineral oil component of lubricants with incidental food contact use on machinery. This chemical is regulated by the FDA as a food additive. The submitted chemistry data has been sent for review.

The goal of this meeting is to determine if any additional assessments need to be completed in order to register this product. This is an internal meeting. Rumor has it that Connie Welch will be the new consultant for this product. I have been told that Jack has agreed to a quick turn around for this registration.

Thanks for your assistance.

Tracy Lantz

↓
I can't get
these ppm to
make sense -
talk to Dennis

Connie, Dennis, Velma, et. all present.

Fee for Service

Ask Dennis ~~MUP~~ or EUP? for Tony's FR Notice

Took to PRIA meeting on 1/27/05

82076-R

Benzoic Acid

PRIA

Why not an EUP and MUP?

One data matrix

Is this 2/4/05 Dennis confirms this is an end use product

Petro-Canada to register MICROL Preservative
$ 90,000 fee has been paid-start date 1/6/05, (due date 12/27/06 ???)
A38 New AI, Food Use, with Exemption → Jackets make a 6 month commitment on this.
Proposed use: to be added to the mineral oil component of lubricants with incidental food contact use on machinery used for producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food, at a maximum level of 0.5% in order to prevent decomposition and odors in the lubricant caused by microorganisms. Highest level of contact with food is: 0.05 ppm.
Previously registered AI, but currently no active registrations containing this AI.
This chemical is regulated by the FDA as a food additive (21 CFR 184.1021 @ 0.1% in food.)
Have a US rep: Elizabeth Brown, Lake Ridge, VA — Elizabeth Brown is leaving this firm
Using the selective method of data support, matrix w/o MRIDs: are all data requirements supported by studies she just sent in?
Label is confusing: discusses finished products and treated articles neither of which can make claims. What finished products/treated articles are they referring to? Examples?
~~Labels should say for formulation or end use product~~
Requests for waivers appear to be in the jacket itself.

using this to formulate lubricants which will have treated articles claims

Don't we need a CSF for the manufacturing process? Submitted CSF just lists the AI and a very small amount on water.

is this in the chemistry study?

Studies submitted:

got this corrected

Product Identity, Composition, and Analysis-REJECTED — got corrections on 2/8/05
Physical & Chemical Properties 46432702
Toxicology 46432703
Ecotoxicology 46432704
Request for Waivers (Ecotoxicology) 46432705
Request for Waivers (Hydrolysis) 46432706
Acute Oral cited RTECS database study
Acute Dermal "
Acute Inhalation "
Primary Eye "
Primary Skin "
Dermal Sensitization cited WHO study
90 day oral rodent "
subchronic nonrodent oral 90 day cited WHO study
dermal tox rodent "
subchronic inhalation toxicity "
develop. tox rodent "
In vitro mutagenicity "
mutagenicity mammalian in culture "

have them define the treated article as the lubricants on the label

using unregistered source

[illegible] chemistry reviewer 3/17/05

start 1/6/05

asked for [illegible] 6/6/05

In vivo cytogenetics	"
Daphnia acute toxicity	"
Acute Toxicity fish	"
Avian Acute toxicity	Justification for waiver
Hydrolysis	Justification for waiver

Their note: sodium benzoate is rapidly metabolized to benzoic acid in mammals. Benzoic acid itself is rapidly metabolized in the liver by conguation with glycine, resulting in formation of hippuric acid, which then is rapidly excreted via the urine. Toxicological data on sodium benzoate can be used to support benzoic acid.

Scoping Meeting of Notes + Attendance Sign in sheet as a record of whatever decision(s) are made.

→ to decide if we need to do a science review

Frank
Jack
Dennis
Velma
~~[illegible]~~
Michele W. (would invite a tox) do we need a tox. review

~~Connie~~ ——

Norm < will invite his branch

give label, matrix, cover letter + background letter prior to meeting
give ≈2 weeks to review materials

get a bottom line @ end of meeting — does it need a RASSB assessment

prepare for meeting: — look for my notes ← did I save electronically? to Dennis?
from previous meeting
present their arguments

does HED have some reviews already? from previous registrations - ask Kay

I should allow myself time to get ready for this meeting

look for all MRID's on this chemical

ChemReg
INTERNATIONAL, LLC

1990 OLD BRIDGE ROAD, SUITE 201
LAKE RIDGE, VIRGINIA 22192-2383

DIRECT: 703-492-7905
MAIN: 703-492-0445
FAX: 703-492-0668

E-MAIL: brown@chemreg.com
WEB SITES: www.chemreg.com
www.pesticide.net

ELIZABETH A. BROWN, PH.D.

464641-00

December 16, 2004

Document Processing Desk (APPL, REGFEE, NEWCO, COADR)
U.S. Environmental Protection Agency (7505C)
Office of Pesticide Programs
Room 266A, Crystal Mall 2
1801 South Bell Street
Arlington, VA 22202-4501

Attn: Velma Noble (PM 31)

Re: Application for Registration of MICROL Preservative
Request for Company Number

Dear Velma:

On behalf of our client, Petro-Canada, Specialty Products and Fluids (Petro-Canada), enclosed please find an application for registration of MICROL Preservative, which contains a new antimicrobial active ingredient.

This application has been previously discussed with the Agency, including discussion on June 5, 2003 for the required approach and multiple discussions and communications during February through May 2004.

This application is subject to PRIA. We believe, based on conversations with Mr. Dennis Edwards, that this application is Fee Category A38, with the associated fee of $90,000. . Please contact me directly at 703-492-7905 or brown@chemreg.com if there any questions regarding the PRIA category.

Enclosed with this application, please find the following:

1. EPA Form 8570-1
2. EPA Form 8570-34, Certification with respect to citation of data
3. EPA Form 8570-35, Data matrix (Agency Use and Public File copies)
4. EPA Form 8570-4, Confidential Statement of Formula
5. A letter from Petro-Canada, requesting a new company number and assigning ChemReg International, LLC, as their US agent
6. Five (5) copies of the proposed labeling
7. Transmittal bibliography
8. Three (3) copies of each submitted study)

If there are any questions or if anything further is needed, please do not hesitate to contact me directly. Please keep me informed of the progress of this application.

Regards,

Elizabeth Anne Brown

Elizabeth Anne Brown

cc: Petro-Canada, Specialty Products and Fluids

TRANSMITTAL DOCUMENT

Submitter
Petro-Canada
Specialty Product and Fluids
2489 North Sheridan Way
Mississauga, Ontario L5K 1A8 CANADA

Regulatory action in support of which this package is submitted
New Product Registration (New Antimicrobial Active Ingredient
(MICROL Preservative, no company number yet assigned)

Transmittal Date
December 16, 2004, 2004

Submitted Studies

	MRID	
----		Administrative Materials
Document 1:	46464101	Brown, E.A. Dec 14, 2004. MICROL Preservative. Product Identity, Composition, and Analysis (Group A). Report No. MICROL-2004-01. ChemReg International, LLC. 77 pages. Contains Business Confidential Information
Document 2:	46432702	Brown, E.A. November 22, 2004. MICROL Preservative. Physical and Chemical Properties (Group B). Report No. MICROL-2004-02 ChemReg International, LLC. 43 pages.
Document 3:	46432703	Brown, E.A. December 6, 2004. MICROL Preservative. Toxicology. Report No. MICROL-2004-03. ChemReg International, LLC. 225 pages
Document 4	46432704	Brown, E.A. Dec 2, 2004 MICROL Preservative. Ecotoxicology. Report No. MICROL-2004-04 ChemReg International, LLC 52 pages.
Document 5	46432705	Brown, E.A. December 2, 2004. MICROL Preservative. Request for Waivers – Ecotoxicology. ChemReg International, LLC. 6 pages.
Document 6	46432706	Brown, E.A. December 2, 2004. MICROL Preservative. Request for Waivers – Hydrolysis. ChemReg International, LLC. 4 pages

Company Official: Elizabeth Anne Brown

Company Name: ChemReg International, LLC., Authorized Agent for Buzz Off Insect Shield

Company Contact: Elizabeth Anne Brown

Phone Number: 703-492-7905

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M STREET, S.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 1.25 hours per response for registration and 0.25 hours per response for reregistration and special review activities, including time for reading the instructions and completing the necessary forms. Send comments regarding burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460.
Do not send the completed form to this address.

Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number	EPA Registration Number/File Symbol
Petro-Canada Specialty Products and Fluids 2489 North Sheridan Way Mississauga, Ontario Canada L5K 1A8 905-804-4500	(not yet assigned) 82076-R
Active Ingredient(s) and/or representative test compound(s) Benzoic Acid	Date 12/14/2004
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158) Indoor Nonfood (material preservative)	Product Name MICROL PRESERVATIVE

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulators Exemption Statement (EPA Form 8570-27)

☐ I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I: METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose)

☒ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

[Required if using the cite-all method, or when using the cite-all option under the selective method to satisfy one or more data requirements]

☐ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA

SECTION III: CERTIFICATION

I certify that this application for registration, this form for reregistration or this Data-Call-In response is supported by all data submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is indicated in Section 1, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identical or similar composition and uses.

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original data submitter or that I have obtained the written permission of the original data submitter to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (i) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title
Elizabeth Anne Brown	12/14/2004	Elizabeth Anne Brown ChemReg International, LLC, Agent for Registrant

EPA Form 8570-34 (9-97) Electronic and Paper versions available. Submit only Paper version.

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and 0.25 hours per response for reregistration and special review activities, including time for reading the instruction and completing the necessary forms. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington DC 20460. Do not send the form to this address.

DATA MATRIX

Date: December 14, 2004		EPA Reg No./ File Symbol (not yet assigned)	Page 1 of 3
Applicant's/Registrant's Name and Address:	Petro-Canada Specialty Products and Fluids 2489 North Sheridan Way Mississauga, Ontario CANADA L5K 1A8	Product: MICROL PRESERVATIVE	
Ingredient: Benzoic Acid			

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
830.1550	Product Identity and composition	46464-01	Petro-Canada	Own	MICROL-2004-01
830.1600	Description of starting materials	46464-01	Petro-Canada	Own	MICROL-2004-01
830.1620	Description of production process	46464-01	Petro-Canada	Own	MICROL-2004-01
830.1670	Discussion of the formation of impurities	46464-01	Petro-Canada	Own	MICROL-2004-01
830.1700	Preliminary analysis	46464-01	Petro-Canada	Own	MICROL-2004-01
830.1750	Certified limits	46464-01	Petro-Canada	Own	MICROL-2004-01
830.1800	Enforcement analytical method	46464-01	Petro-Canada	Own	MICROL-2004-01
830.6302	Color	464327-02	Petro-Canada	Own	MICROL-2004-02
830.6303	Physical state	464327-02	Petro-Canada	Own	MICROL-2004-02
830.6304	Odor	464327-02	Petro-Canada	Own	MICROL-2004-02
830.6313	Stability	464327-02	Petro-Canada	Own	MICROL-2004-02
830.6314	Oxidation/reduction	464327-02	Petro-Canada	Own	MICROL-2004-02
830.6315	Flammability	464327-02	Petro-Canada	Own	MICROL-2004-02
830.6316	Explodability	464327-02	Petro-Canada	Own	MICROL-2004-02
830.6317	Storage stability	464327-02	Petro-Canada	Own	MICROL-2004-02
830.6319	Miscibility	464327-02	Petro-Canada	Own	MICROL-2004-02
830.6320	Corrosion characteristics	464327-02	Petro-Canada	Own	MICROL-2004-02
830.6321	Dielectric breakdown voltage	464327-02	Petro-Canada	Own	MICROL-2004-02

Signature	Name and Title	Date
Elizabeth Anne Brown	Elizabeth Anne Brown ChemReg International, LLC, agent for Petro Canada	12/14/2004

EPA Form 8570-35 (9-97) Electronic and Paper versions available. Submit only Paper version.

Agency Internal Use Copy

Disuss/make corrections
to data matrix

END

13:18:07

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and 0.25 hours per response for reregistration and special review activities, including time for reading the instruction and completing the necessary forms. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington DC 20460. Do not send the form to this address.

DATA MATRIX

Date: December 14, 2004		EPA Reg No./ File Symbol (not yet assigned)	Page 2 of 3
Applicant's/Registrant's Name and Address:	Petro-Canada Specialty Products and Fluids 2489 North Sheridan Way Mississauga, Ontario CANADA L5K 1A8	Product: MICROL PRESERVATIVE	
Ingredient: Benzoic Acid			

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
830.7000	pH	464327-02	Petro-Canada	Own	MICROL-2004-02
830.7050	UV/Vis absorption	464327-02	Petro-Canada	Own	MICROL-2004-02
830.7100	Viscosity	464327-02	Petro-Canada	Own	MICROL-2004-02
830.7200	Melting point	464327-02	Petro-Canada	Own	MICROL-2004-02
830.7220	Boiling point	464327-02	Petro-Canada	Own	MICROL-2004-02
830.7300	Density	464327-02	Petro-Canada	Own	MICROL-2004-02
830.7370	Dissociation constant	464327-02	Petro-Canada	Own	MICROL-2004-02
830.7550	Octanol/water partition coefficient	464327-02	Petro-Canada	Own	MICROL-2004-02
830.7840	Solubility	464327-02	Petro-Canada	Own	MICROL-2004-02
830.7950	Vapor pressure	464327-02	Petro-Canada	Own	MICROL-2004-02
870.1100	Acute oral toxicity		Petro-Canada	Own	MICROL-2004-03
870.1200	Acute dermal toxicity		Petro-Canada	Own	MICROL-2004-03
870.1300	Acute inhalation toxicity		Petro-Canada	Own	MICROL-2004-03
870.2400	Primary eye irritation		Petro-Canada	Own	MICROL-2004-03
870.2500	Primary dermal irritation		Petro-Canada	Own	MICROL-2004-03
870.2600	Dermal sensitization		Petro-Canada	Own	MICROL-2004-03
870.3100	90-day oral toxicity - rodent		Petro-Canada	Own	MICROL-2004-03
870.3150	90-day oral toxicity - nonrodent		Petro-Canada	Own	MICROL-2004-03

Signature	Name and Title	Date
Elizabeth Anne Brown	Elizabeth Anne Brown ChemReg International, LLC, agent for Petro Canada	12/14/2004

EPA Form 8570-35 (9-97) Electronic and Paper versions available. Submit only Paper version.

Agency Internal Use Copy

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and 0.25 hours per response for reregistration and special review activities, including time for reading the instruction and completing the necessary forms. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington DC 20460. Do not send the form to this address.

DATA MATRIX

Date: December 14, 2004		EPA Reg No./ File Symbol (not yet assigned)	Page 3 of 3
Applicant's/Registrant's Name and Address:	Petro-Canada Specialty Products and Fluids 2489 North Sheridan Way Mississauga, Ontario CANADA L5K 1A8	Product: MICROL PRESERVATIVE	
Ingredient: Benzoic Acid			

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
870.3250	Repeat dose dermal toxicity		Petro-Canada	Own	MICROL-2004-03
870.3465	Subchronic inhalation toxicity		Petro-Canada	Own	MICROL-2004-03
870.3700	Developmental toxicity		Petro-Canada	Own	MICROL-2004-03
870.3800	Reproductive toxicity		Petro-Canada	Own	MICROL-2004-03
870.5100	Mutagenicity – bacterial gene mutation		Petro-Canada	Own	MICROL-2004-03
870.5265	In vitro mutagenicity		Petro-Canada	Own	MICROL-2004-03
870.5300	Mutagenicity – mammalian cells in culture		Petro-Canada	Own	MICROL-2004-03
870.5380	In vivo cytogenetics		Petro-Canada	Own	MICROL-2004-03
850.1010	Daphnia acute toxicity		Petro-Canada	Own	MICROL-2004-04
850.1075	Acute toxicity – fish		Petro-Canada	Own	MICROL-2004-04
850.2100	Avian acute toxicity		Petro-Canada	Own	MICROL-2004-05
835.2120	Hydrolysis		Petro-Canada	Own	MICROL-2004-06

Signature 143 Elizabeth Anne Brown	Name and Title Elizabeth Anne Brown ChemReg International, LLC, agent for Petro Canada	Date 12/14/2004

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and 0.25 hours per response for reregistration and special review activities, including time for reading the instruction and completing the necessary forms. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington DC 20460. Do not send the form to this address.

DATA MATRIX

Date: December 14, 2004		EPA Reg No./ File Symbol (not yet assigned)	Page 1 of 3
Applicant's/Registrant's Name and Address:	Petro-Canada Specialty Products and Fluids 2489 North Sheridan Way Mississauga, Ontario CANADA L5K 1A8	Product: MICROL PRESERVATIVE	
Ingredient: Benzoic Acid			

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]			Petro-Canada	Own	MICROL-2004-01
			Petro-Canada	Own	MICROL-2004-01
			Petro-Canada	Own	MICROL-2004-01
			Petro-Canada	Own	MICROL-2004-01
			Petro-Canada	Own	MICROL-2004-01
			Petro-Canada	Own	MICROL-2004-01
			Petro-Canada	Own	MICROL-2004-01
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02

Signature	Name and Title	Date
Elizabeth Anne Brown	Elizabeth Anne Brown ChemReg International, LLC, agent for Petro Canada	12/14/2004

EPA Form 8570-35 (9-97) Electronic and Paper versions available. Submit only Paper version.

Public File Copy

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and 0.25 hours per response for reregistration and special review activities, including time for reading the instruction and completing the necessary forms. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington DC 20460. Do not send the form to this address.

DATA MATRIX

Date: December 14, 2004		EPA Reg No./ File Symbol (not yet assigned)	Page 2 of 3
Applicant's/Registrant's Name and Address:	Petro-Canada Specialty Products and Fluids 2489 North Sheridan Way Mississauga, Ontario CANADA L5K 1A8	Product: MICROL PRESERVATIVE	
Ingredient: Benzoic Acid			

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-02
			Petro-Canada	Own	MICROL-2004-03
			Petro-Canada	Own	MICROL-2004-03
			Petro-Canada	Own	MICROL-2004-03
			Petro-Canada	Own	MICROL-2004-03
			Petro-Canada	Own	MICROL-2004-03
			Petro-Canada	Own	MICROL-2004-03
			Petro-Canada	Own	MICROL-2004-03
			Petro-Canada	Own	MICROL-2004-03

Signature	Name and Title	Date
Elizabeth Anne Brown	Elizabeth Anne Brown ChemReg International, LLC, agent for Petro Canada	12/14/2004

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and 0.25 hours per response for reregistration and special review activities, including time for reading the instruction and completing the necessary forms. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington DC 20460. Do not send the form to this address.

DATA MATRIX

Date: December 14, 2004		EPA Reg No./ File Symbol (not yet assigned)	Page 3 of 3
Applicant's/Registrant's Name and Address:	Petro-Canada Specialty Products and Fluids 2489 North Sheridan Way Mississauga, Ontario CANADA L5K 1A8	Product: MICROL PRESERVATIVE	
Ingredient: Benzoic Acid			

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]			Petro-Canada	Own	MICROL-2004-03
			Petro-Canada	Own	MICROL-2004-03
			Petro-Canada	Own	MICROL-2004-03
			Petro-Canada	Own	MICROL-2004-03
			Petro-Canada	Own	MICROL-2004-03
			Petro-Canada	Own	MICROL-2004-03
			Petro-Canada	Own	MICROL-2004-03
			Petro-Canada	Own	MICROL-2004-03
			Petro-Canada	Own	MICROL-2004-04
			Petro-Canada	Own	MICROL-2004-04
			Petro-Canada	Own	MICROL-2004-05
			Petro-Canada	Own	MICROL-2004-06

Signature	Name and Title	Date
Elizabeth Anne Brown	Elizabeth Anne Brown ChemReg International, LLC, agent for Petro Canada	12/14/2004

EPA Form 8570-35 (9-97) Electronic and Paper versions available. Submit only Paper version.

Public File Copy

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

February 10, 2005

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

CHEMREG INTERNATIONAL LLC
PETRO-CANADA
1990 OLD BRIDGE ROAD, SUITE 201
LAKE RIDGE, VA 22191-2383

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your submittal of 09-FEB-05. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 86-5. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.

United States Environmental Protection Agency

Washington, D.C. 20460

Office of Prevention, Pesticides and Toxic Substances

Office of Pesticide Programs

Antimicrobial Division

FAX NUMBER(703) 308- 8481

FACSIMILE REQUEST/COVER SHEET

(Please type or print clearly in black ink only)

SEND FAX TO:

Name: Elizabeth Brown

Office: Chem Reg

FAX Phone No. 703 492 0668

FROM:

Name: Tracy Lantz

Division/Branch: AD

Office Phone No. 703 308 6415

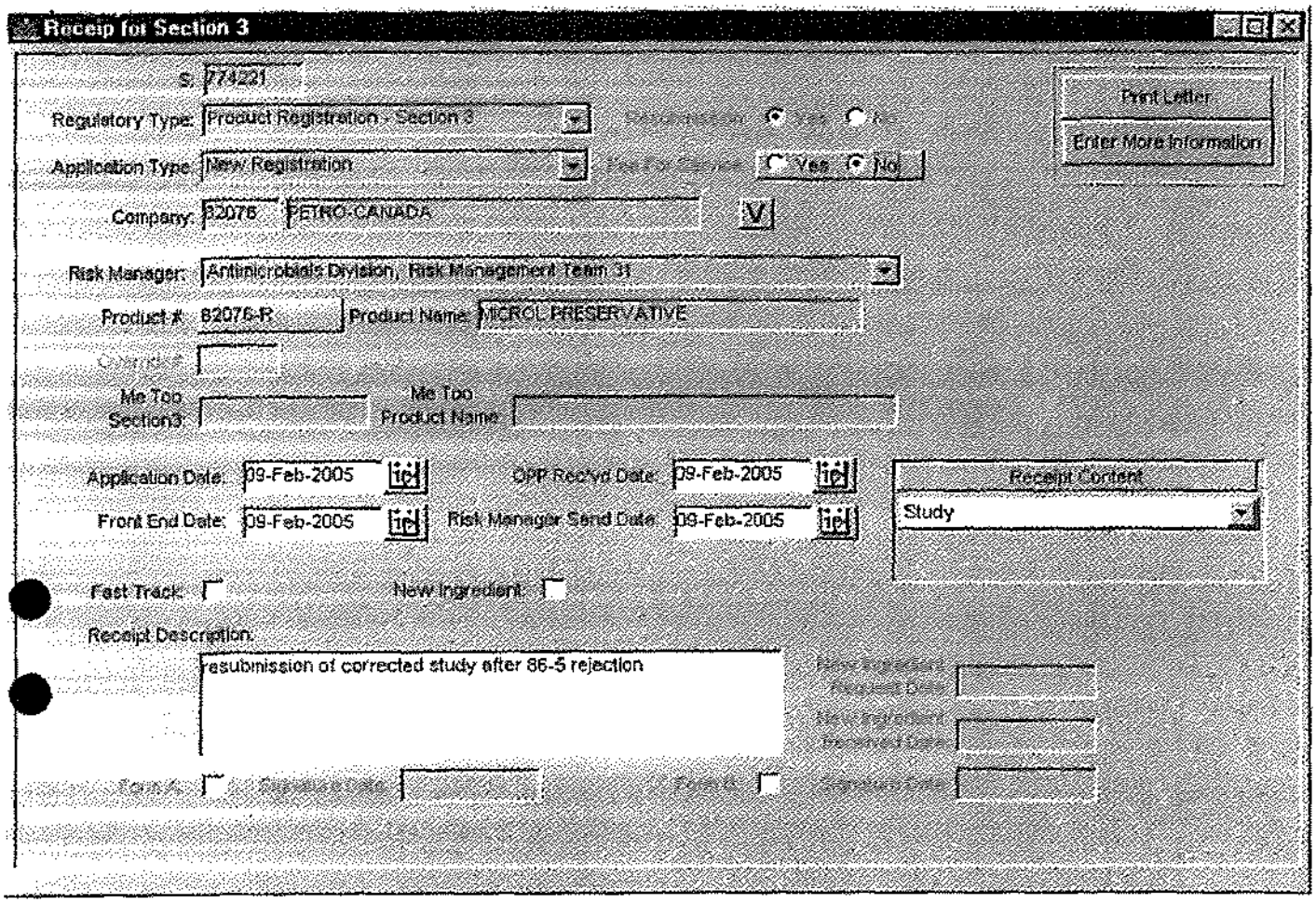
Office Room No.

Mail Code: 7510 C Date: 2/17/05 Time: 4:15 PM

Number of pages (with this cover sheet): 5

Special Message:

Copy of 86-5 compliance + MRID assignments


Receip for Section 3
S 774221
Regulatory Type: Product Registration - Section 3
Application Type: New Registration
Company: 62076 PETRO-CANADA
Risk Manager: Antimicrobials Division, Risk Management Team 31
Product #: 62076-R
Product Name: MICROL PRESERVATIVE
Me Too Section3:
Me Too Product Name:
Application Date: 09-Feb-2005
OPP Rec'vd Date: 09-Feb-2005
Front End Date: 09-Feb-2005
Risk Manager Send Date: 09-Feb-2005
Fast Track:
New Ingredient:
Receipt Description:
resubmission of corrected study after 86-5 rejection
Print Letter
Enter More Information
Yes
No
Receipt Content
Study

Administrative Materials

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

PM 31

December 29, 2004

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

PETRO-CANADA
1990 OLD BRIDGE ROAD, SUITE 20[illegible]
LAKE RIDGE, VA 22191-2383

Studies came in with 82076-R

2/8/05 Studies corrected

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your submittal of 16-DEC-04. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your data submittal was found to be partially in compliance with the standards for submission of data contained in PR Notice 86-5, with the exceptions noted below. A copy of your transmittal bibliography is enclosed, annotated with the Master Record ID's (MRIDs) assigned to each document accepted. Please use these numbers in all future references to these documents.

If deficiencies were found which apply to individual accepted studies, they are listed below following the applicable MRID. Any document which has been assigned a MRID has been accepted under PR Notice 86-5. If any comments related to a MRID appear on this report, they are provided for your information and reference when preparing future submissions. Some individual documents were not acceptable, and all copies are being returned to you for correction for the reasons indicated below.

These rejected studies have been assigned separate identification numbers which are annotated on both the enclosed bibliography and the rejected document labels

The rejected studies and their deficiencies are described below

Rejected Study [01]:

* The presence of a Confidential Attachment causes a direct conflict with the No Claim of Confidentiality statement. (See Confidential Attachment Page 23)

ChemReg
INTERNATIONAL, LLC

464327-00

1990 OLD BRIDGE ROAD, SUITE 201
LAKE RIDGE, VIRGINIA 22192-2383

DIRECT: 703-492-7905
MAIN: 703-492-0445
FAX: 703-492-0668

E-MAIL: brown@chemreg.com
WEB SITES: www.chemreg.com
www.pesticide.net

ELIZABETH A. BROWN, PH.D.

December 16, 2004

Document Processing Desk (APPL, REGFEE, NEWCO, COADR)
U.S. Environmental Protection Agency (7505C)
Office of Pesticide Programs
Room 266A, Crystal Mall 2
1801 South Bell Street
Arlington, VA 22202-4501

Attn: Velma Noble (PM 31)

Re: Application for Registration of MICROL Preservative
Request for Company Number

Dear Velma:

On behalf of our client, Petro-Canada, Specialty Products and Fluids (Petro-Canada), enclosed please find an application for registration of MICROL Preservative, which contains a new antimicrobial active ingredient.

This application has been previously discussed with the Agency, including discussion on June 5, 2003 for the required approach and multiple discussions and communications during February through May 2004.

This application is subject to PRIA. We believe, based on conversations with Mr. Dennis Edwards, that this application is Fee Category A38, with the associated fee of $90,000. . Please contact me directly at 703-492-7905 or brown@chemreg.com if there any questions regarding the PRIA category.

ChemReg
INTERNATIONAL, LLC

Enclosed with this application, please find the following:

1. EPA Form 8570-1
2. EPA Form 8570-34, Certification with respect to citation of data
3. EPA Form 8570-35, Data matrix (Agency Use and Public File copies)
4. EPA Form 8570-4, Confidential Statement of Formula
5. A letter from Petro-Canada, requesting a new company number and assigning ChemReg International, LLC, as their US agent
6. Five (5) copies of the proposed labeling
7. Transmittal bibliography
8. Three (3) copies of each submitted study)

If there are any questions or if anything further is needed, please do not hesitate to contact me directly. Please keep me informed of the progress of this application.

Regards,

Elizabeth Anne Brown

Elizabeth Anne Brown

cc: Petro-Canada, Specialty Products and Fluids

TRANSMITTAL DOCUMENT

Submitter

Petro-Canada
Specialty Product and Fluids
2489 North Sheridan Way
Mississauga, Ontario L5K 1A8 CANADA

Regulatory action in support of which this package is submitted

New Product Registration (New Antimicrobial Active Ingredient
(MICROL Preservative, no company number yet assigned)

Transmittal Date

December 16, 2004, 2004

Submitted Studies

	MRID	
---		Administrative Materials
Document 1:	Reject (01)	Brown, E.A. Dec 14, 2004. MICROL Preservative. Product Identity, Composition, and Analysis (Group A). Report No. MICROL-2004-01. ChemReg International, LLC. 77 pages. Contains Business Confidential Information
Document 2:	46432702	Brown, E.A. November 22, 2004. MICROL Preservative. Physical and Chemical Properties (Group B). Report No. MICROL-2004-02. ChemReg International, LLC. 43 pages.
Document 3:	46432703	Brown, E.A. December 6, 2004. MICROL Preservative. Toxicology. Report No. MICROL-2004-03. ChemReg International, LLC. 225 pages.
Document 4	46432704	Brown, E.A. Dec 2, 2004. MICROL Preservative. Ecotoxicology. Report No. MICROL-2004-04. ChemReg International, LLC. 52 pages.
Document 5	46432705	Brown, E.A. December 2, 2004. MICROL Preservative. Request for Waivers – Ecotoxicology. ChemReg International, LLC. 6 pages.
Document 6	46432706	Brown, E.A. December 2, 2004. MICROL Preservative. Request for Waivers – Hydrolysis. ChemReg International, LLC. 4 pages

Company Official: Elizabeth Anne Brown

Company Name: ChemReg International, LLC., Authorized Agent for Buzz Off Insect Shield

Company Contact: Elizabeth Anne Brown

Phone Number: 703-492-7905

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

December 29, 2004

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

PETRO-CANADA
1990 OLD BRIDGE ROAD, SUITE 201
LAKE RIDGE, VA 22191-2383

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your submittal of 16-DEC-04. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your data submittal was found to be partially in compliance with the standards for submission of data contained in PR Notice 86-5, with the exceptions noted below. A copy of your transmittal bibliography is enclosed, annotated with the Master Record ID's (MRIDs) assigned to each document accepted. Please use these numbers in all future references to these documents.

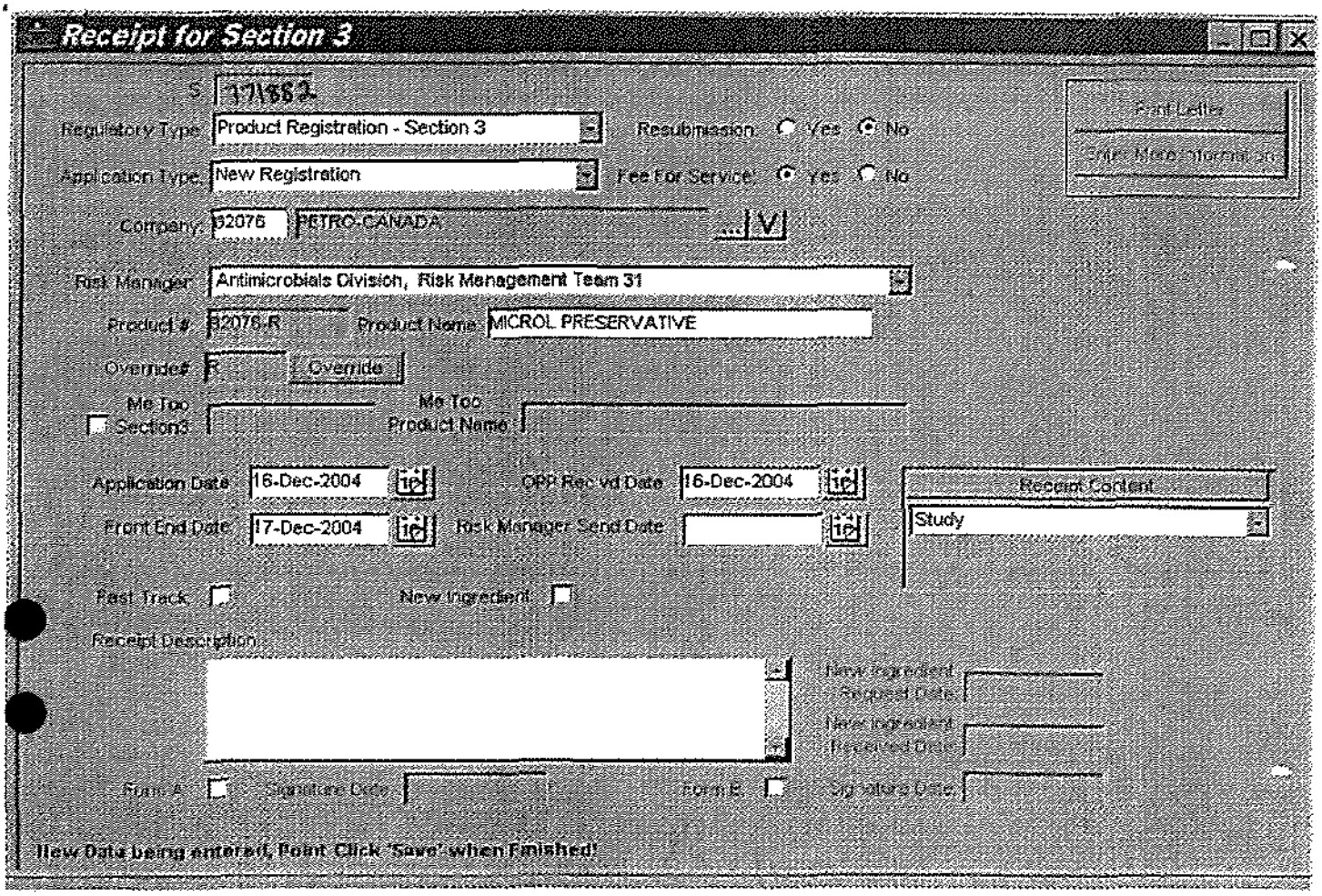
If deficiencies were found which apply to individual accepted studies, they are listed below following the applicable MRID. Any document which has been assigned a MRID has been accepted under PR Notice 86-5. If any comments related to a MRID appear on this report, they are provided for your information and reference when preparing future submissions. Some individual documents were not acceptable, and all copies are being returned to you for correction for the reasons indicated below.

These rejected studies have been assigned separate identification numbers which are annotated on both the enclosed bibliography and the rejected document labels.

The rejected studies and their deficiencies are described below.

Rejected Study [01]:

* The presence of a Confidential Attachment causes a direct conflict with the No Claim of Confidentiality statement. (See Confidential Attachment Page 23)


Receipt for Section 3
S 37882
Regulatory Type: Product Registration - Section 3
Resubmission: Yes No
Application Type: New Registration
Fee For Service: Yes No
Company: 62076 PETRO-CANADA
Risk Manager: Antimicrobials Division, Risk Management Team 31
Product #: 62076-R
Product Name: MICROL PRESERVATIVE
Override#: R
Override
Me Too Section3
Me Too Product Name
Application Date: 16-Dec-2004
OPP Recvd Date: 16-Dec-2004
Front End Date: 17-Dec-2004
Risk Manager Send Date:
Receipt Content
Study
Fast Track:
New Ingredient:
Receipt Description:
Form A:
Signature Date:
Form B:
New Data being entered, Point Click 'Save' when Finished!

ChemReg
INTERNATIONAL, LLC

464327-00

1990 OLD BRIDGE ROAD, SUITE 201
LAKE RIDGE, VIRGINIA 22192-2383

DIRECT: 703-492-7905
MAIN: 703-492-0445
Fax: 703-492-0668

E-MAIL: brown@chemreg.com
WEB SITES: www.chemreg.com
www.pesticide.net

ELIZABETH A. BROWN, PH.D.

December 16, 2004

Document Processing Desk (APPL, REGFEE, NEWCO, COADR)
U.S. Environmental Protection Agency (7505C)
Office of Pesticide Programs
Room 266A, Crystal Mall 2
1801 South Bell Street
Arlington, VA 22202-4501

Attn: Velma Noble (PM 31)

Re: Application for Registration of MICROL Preservative
Request for Company Number

Dear Velma:

On behalf of our client, Petro-Canada, Specialty Products and Fluids (Petro-Canada), enclosed please find an application for registration of MICROL Preservative, which contains a new antimicrobial active ingredient.

This application has been previously discussed with the Agency, including discussion on June 5, 2003 for the required approach and multiple discussions and communications during February through May 2004.

This application is subject to PRIA. We believe, based on conversations with Mr. Dennis Edwards, that this application is Fee Category A38, with the associated fee of $90,000. . Please contact me directly at 703-492-7905 or brown@chemreg.com if there any questions regarding the PRIA category.

Enclosed with this application, please find the following:

1. EPA Form 8570-1
2. EPA Form 8570-34, Certification with respect to citation of data
3. EPA Form 8570-35, Data matrix (Agency Use and Public File copies)
4. EPA Form 8570-4, Confidential Statement of Formula
5. A letter from Petro-Canada, requesting a new company number and assigning ChemReg International, LLC, as their US agent
6. Five (5) copies of the proposed labeling
7. Transmittal bibliography
8. Three (3) copies of each submitted study)

If there are any questions or if anything further is needed, please do not hesitate to contact me directly. Please keep me informed of the progress of this application.

Regards,

Elizabeth Anne Brown

Elizabeth Anne Brown

cc: Petro-Canada, Specialty Products and Fluids

TRANSMITTAL DOCUMENT

Submitter
Petro-Canada
Specialty Product and Fluids
2489 North Sheridan Way
Mississauga, Ontario L5K 1A8 CANADA

Regulatory action in support of which this package is submitted
New Product Registration (New Antimicrobial Active Ingredient
(MICROL Preservative, no company number yet assigned)

Transmittal Date
December 16, 2004, 2004

Submitted Studies

	MRID	
----		Administrative Materials
Document 1:	Reject (01)	Brown, E.A. Dec 14, 2004. MICROL Preservative. Product Identity, Composition, and Analysis (Group A). Report No. MICROL-2004-01. ChemReg International, LLC. 77 pages. Contains Business Confidential Information
Document 2:	46432702	Brown, E.A. November 22, 2004. MICROL Preservative. Physical and Chemical Properties (Group B). Report No. MICROL-2004-02. ChemReg International, LLC. 43 pages.
Document 3:	46432703	Brown, E.A. December 6, 2004. MICROL Preservative. Toxicology. Report No. MICROL-2004-03. ChemReg International, LLC. 225 pages.
Document 4	46432704	Brown, E.A. Dec 2, 2004. MICROL Preservative. Ecotoxicology. Report No. MICROL-2004-04. ChemReg International, LLC. 52 pages.
Document 5	46432705	Brown, E.A. December 2, 2004. MICROL Preservative. Request for Waivers – Ecotoxicology. ChemReg International, LLC. 6 pages.
Document 6	46432706	Brown, E.A. December 2, 2004. MICROL Preservative. Request for Waivers – Hydrolysis. ChemReg International, LLC. 4 pages

Company Official Elizabeth Anne Brown

Company Name: ChemReg International, LLC., Authorized Agent for Buzz Off Insect Shield

Company Contact: Elizabeth Anne Brown

Phone Number: 703-492-7905

Title

MICROL Preservative: Request for Waivers

Data Requirements

OPPTS 850.2100 Avian acute toxicity

Author

E. A. Brown
ChemReg International, LLC
1990 Old Bridge Road, Suite 201
Lake Ridge, VA 20192

Sponsor

Petro-Canada
Specialty Products and Fluids
2489 North Sheridan Way
Mississauga, Ontario Canada L5K 1A8

Study Completion Date

December 2, 2004

Report Number

MICROL-2004-05

Total pages: 6

Statement of Data Confidentiality Claim

No information is claimed confidential on the basis of its falling within the scope of FIFRA § 10(d)(1)(A), (B), or (C).

Company: Petro-Canada
Specialty Products and Fluids

Submitter Name: Elizabeth Anne Brown
ChemReg International, LLC
Authorized Agent for Petro-Canada

Signed: Elizabeth Anne Brown

Date: December 2, 2004

Good Laboratory Practices Statement

The submitter of this study was neither the sponsor of this study nor conducted it, and does not know whether it has been conducted in accordance with 40 CFR Part 160.

Author Submitter: Elizabeth Anne Brown Date: Dec 2, 2004

Elizabeth Anne Brown
ChemReg International, LLC

OPPTS 850.2100 Avian Acute Toxicity

A from the requirement to conduct a study to determine the acute toxicity of MICROL Preservative is requested. MICROL Preservative is 100% USP grade benzoic acid, an extremely well-known direct food additive and preservative. The proposed use is indoor, nonfood, as an antimicrobial additive to lubricating oils used in food processing equipment. While it and the very closely related sodium benzoate have been extensively researched and are ubiquitous in nature, there are no known studies to determine the acute oral toxicity of either compound to birds. However, there are adequate bases for determining that such a study can be waived without unreasonable adverse effect.

Natural occurrence of Benzoic Acid: (as cited from WHO 2000)

"Benzoic acid is produced by many plants as an intermediate in the formation of other compounds (Goodwin, 1976). High concentrations are found in certain berries.... Benzoic acid has also been detected in animals (see section 6.1). Benzoic acid therefore occurs naturally in many foods, including milk products (Sieber et al., 1989, 1990)."

"Generally, benzoic acid can occur in almost all environmental compartments. Whether it exists in the undissociated or dissociated form depends on the specific physicochemical conditions. Above pH 6, the benzoate anion prevails (Chipley, 1983)."

"Benzoic acid occurs naturally in free and bound form in many plant and animal species. It is a common metabolite in plants and organisms (Hegnauer, 1992). Appreciable amounts have been found in gum benzoin (around 20%) and most berries (around 0.05%) (Budavari et al., 1996). For example, ripe fruits of several *Vaccinium* species (e.g., cranberry, *V. vitis idaea*; bilberry, *V. macrocarpon)* contain as much as 300-1300 mg free benzoic acid per kg fruit (Hegnauer, 1966). Benzoic acid is also formed in apples after infection with the fungus *Nectria galligena* (Harborne, 1983) or in *Pinus thunbergii* callus inoculated with a pathogenic pine wood nematode *(Bursaphelenchus xylophilus)* (Zhang et al., 1997). Among animals, benzoic acid has been identified primarily in omnivorous or phytophageous species, e.g., in viscera and muscles of the ptarmigan *(Lagopus mutus)* (Hegnauer, 1989) as well as in gland secretions of male muskoxen *(Ovibos moschatus)* (Flood et al., 1989) or Asian bull elephants *(Elephas maximus)* (Rasmussen et al., 1990)."

"Owing to its occurrence in many organisms, benzoic acid is naturally present in foods (review in Sieber et al., 1989, 1990). Some typical examples specifying reported ranges of means in selected foods have been compiled from Sieber et al. (1989) as follows:

Milk	traces - 6 mg/kg
Yoghurt	12-40 mg/kg
Cheese	traces - 40 mg/kg
Fruits (excluding *Vaccinium* species)	traces - 14 mg/kg
Potatoes, beans, cereals	traces - 0.2 mg/kg
Soya flour, nuts	1.2-11 mg/kg

"Honeys from different floral sources ($n = 7$) were found to contain free benzoic acid at concentrations of <10 mg/kg ($n = 5$) and of <100 mg/kg ($n = 2$) (Steeg & Montag, 1987)."

Acute toxicity of Benzoic Acid to Mammals and Relation to Birds

"After oral uptake, benzoic acid and sodium benzoate are rapidly absorbed from the gastrointestinal tract and metabolized in the liver by conjugation with glycine, resulting in the formation of hippuric acid, which is rapidly excreted via the urine. To a lesser extent, benzoates applied dermally can penetrate through the skin. Owing to rapid metabolism and excretion, an accumulation of the benzoates or their metaholites is not to be expected." (WHO 2000)

"In the acid conditions of the stomach, the equilibrium moves to the undissociated benzoic acid molecule, which should be absorbed rapidly. Benzoate from sodium benzoate would change from the ionized form to the undissociated benzoic acid molecule. As a result, the metabolism and systemic effects of benzoic acid and sodium benzoate can be evaluated together." (WHO 2000)

WHO 1996 reports that birds metabolize benzoic acid acid and sodium benzoate in a similar manner to man and other mammal, with rapid exrection primarily as hippuric acid.

The acute oral LD50 of benzoic acid to rats is 2000-2500 mg/kg bw (Ignat'ev (1965), as cited in WHO 1996). According to the RTECS Database for Benzoic acid (RTECS # DG0875000), the acute oral LD50 in rats is 1,700 mg/kg bw (as cited by NIOSH, 2004).

"With oral LD_{50} values (administration by gavage) of 3040 mg benzoic acid/kg body weight in rats (Bio-Fax, 1973) and 1940-2263 mg benzoic acid/kg body weight in mice (McCormick, 1974; Abe et al., 1984), the acute toxicity of benzoic acid is low. Clinical signs of intoxication (reported for rats only) included diarrhoea, muscular weakness, tremors, hypoactivity, and emaciation (Bio-Fax, 1973). With oral LD_{50} values of 2100-4070 mg sodium benzoate/kg body weight in rats, the acute toxicity of sodium benzoate is similar to that of benzoic acid, as are the symptoms (Smyth & Carpenter, 1948; Deuel et al., 1954; Bayer AG, 1977)." (as cited in WHO 2000).

With similar metabolism to mammals, and with the known low toxicity of benzoic acid to mammals, there is no reason to anticipate that this compound would be more toxic to birds. In fact, benzoic acid often is added as a preservative to poultry feed at levels not exceeding 0.1%. The acute toxicity to birds is expected to be similar to that in mammals, or approximately at the limit dose required in OPPTS 870.2100.

Conclusion
On the basis of the above, it can be reliably concluded that benzoic acid will be of a low order of acute toxicity to avian species. Birds such as would be used in conducting a study (either Northern bobwhite, *Colinus virginianus* (L.), or mallard, *Anas platyrhynchos* L.) are exposed to high environmental levels of benzoic acid, with no known adverse effects ever having been reported. Benzoic acid can be considered to present little hazard to avian species from the proposed use of MICROL Preservative.

References: (full reports are included in Petro-Canada Report MICROL-2004-03)

WORLD HEALTH ORGANIZATION. 2000. CONCISE INTERNATIONAL CHEMICAL ASSESSMENT DOCUMENT NO. 26. ENZOIC ACID AND SODIUM BENZOATE

WORLD HEALTH ORGANIZATION. 1996. BENZYL ACETATE, BENZYL ALCOHOL, BENZALDEHYDE, AND BENZOIC ACID AND ITS SALTS. TOXICOLOGICAL EVALUATION OF CERTAIN FOOD ADDITIVES. Prepared by the 46th meeting of the Joint FAO/WHO Expert Committee on Food Additives (JEFCA). WHO Food Additives Series 37

NIOSH. 2004. RTECS Database for Benzoic Acid

Title

MICROL Preservative: Request for Waivers

Data Requirements

OPPTS 850.2100 Avian acute toxicity

Author

E. A. Brown
ChemReg International, LLC
1990 Old Bridge Road, Suite 201
Lake Ridge, VA 20192

Sponsor

Petro-Canada
Specialty Products and Fluids
2489 North Sheridan Way
Mississauga, Ontario Canada L5K 1A8

Study Completion Date

December 2, 2004

Report Number

MICROL-2004-05

Total pages: 6

Statement of Data Confidentiality Claim

No information is claimed confidential on the basis of its falling within the scope of FIFRA § 10(d)(1)(A), (B), or (C).

Company: Petro-Canada
Specialty Products and Fluids

Submitter Name: Elizabeth Anne Brown
ChemReg International, LLC
Authorized Agent for Petro-Canada

Signed: Elizabeth Anne Brown

Date: December 2, 2004

Good Laboratory Practices Statement

The submitter of this study was neither the sponsor of this study nor conducted it, and does not know whether it has been conducted in accordance with 40 CFR Part 160.

Author Submitter: Elizabeth Anne Brown Date: Dec 2, 2004

Elizabeth Anne Brown
ChemReg International, LLC

OPPTS 850.2100 Avian Acute Toxicity

A from the requirement to conduct a study to determine the acute toxicity of MICROL Preservative is requested. MICROL Preservative is 100% USP grade benzoic acid, an extremely well-known direct food additive and preservative. The proposed use is indoor, nonfood, as an antimicrobial additive to lubricating oils used in food processing equipment. While it and the very closely related sodium benzoate have been extensively researched and are ubiquitous in nature, there are no known studies to determine the acute oral toxicity of either compound to birds. However, there are adequate bases for determining that such a study can be waived without unreasonable adverse effect.

Natural occurrence of Benzoic Acid: (as cited from WHO 2000)

"Benzoic acid is produced by many plants as an intermediate in the formation of other compounds (Goodwin, 1976). High concentrations are found in certain berries.... Benzoic acid has also been detected in animals (see section 6.1). Benzoic acid therefore occurs naturally in many foods, including milk products (Sieber et al., 1989, 1990)."

"Generally, benzoic acid can occur in almost all environmental compartments. Whether it exists in the undissociated or dissociated form depends on the specific physicochemical conditions. Above pH 6, the benzoate anion prevails (Chipley, 1983)."

"Benzoic acid occurs naturally in free and bound form in many plant and animal species. It is a common metabolite in plants and organisms (Hegnauer, 1992). Appreciable amounts have been found in gum benzoin (around 20%) and most berries (around 0.05%) (Budavari et al., 1996). For example, ripe fruits of several *Vaccinium* species (e.g., cranberry, *V. vitis idaea*; bilberry, *V. macrocarpon)* contain as much as 300-1300 mg free benzoic acid per kg fruit (Hegnauer, 1966). Benzoic acid is also formed in apples after infection with the fungus *Nectria galligena* (Harborne, 1983) or in *Pinus thunbergii* callus inoculated with a pathogenic pine wood nematode *(Bursaphelenchus xylophilus)* (Zhang et al., 1997). Among animals, benzoic acid has been identified primarily in omnivorous or phytophageous species, e.g., in viscera and muscles of the ptarmigan *(Lagopus mutus)* (Hegnauer, 1989) as well as in gland secretions of male muskoxen *(Ovibos moschatus)* (Flood et al., 1989) or Asian bull elephants *(Elephas maximus)* (Rasmussen et al., 1990)."

"Owing to its occurrence in many organisms, benzoic acid is naturally present in foods (review in Sieber et al., 1989, 1990). Some typical examples specifying reported ranges of means in selected foods have been compiled from Sieber et al. (1989) as follows:

Milk	traces - 6 mg/kg
Yoghurt	12-40 mg/kg
Cheese	traces - 40 mg/kg
Fruits (excluding *Vaccinium* species)	traces - 14 mg/kg
Potatoes, beans, cereals	traces - 0.2 mg/kg
Soya flour, nuts	1.2-11 mg/kg

"Honeys from different floral sources ($n = 7$) were found to contain free benzoic acid at concentrations of <10 mg/kg ($n = 5$) and of <100 mg/kg ($n = 2$) (Steeg & Montag, 1987)."

Acute toxicity of Benzoic Acid to Mammals and Relation to Birds

"After oral uptake, benzoic acid and sodium benzoate are rapidly absorbed from the gastrointestinal tract and metabolized in the liver by conjugation with glycine, resulting in the formation of hippuric acid, which is rapidly excreted via the urine. To a lesser extent, benzoates applied dermally can penetrate through the skin. Owing to rapid metabolism and excretion, an accumulation of the benzoates or their metabolites is not to be expected." (WHO 2000)

"In the acid conditions of the stomach, the equilibrium moves to the undissociated benzoic acid molecule, which should be absorbed rapidly. Benzoate from sodium benzoate would change from the ionized form to the undissociated benzoic acid molecule. As a result, the metabolism and systemic effects of benzoic acid and sodium benzoate can be evaluated together." (WHO 2000)

WHO 1996 reports that birds metabolize benzoic acid acid and sodium benzoate in a similar manner to man and other mammal, with rapid excretion primarily as hippuric acid.

The acute oral LD50 of benzoic acid to rats is 2000-2500 mg/kg bw (Ignat'ev (1965), as cited in WHO 1996). According to the RTECS Database for Benzoic acid (RTECS # DG0875000), the acute oral LD50 in rats is 1,700 mg/kg bw (as cited by NIOSH, 2004).

"With oral LD_{50} values (administration by gavage) of 3040 mg benzoic acid/kg body weight in rats (Bio-Fax, 1973) and 1940-2263 mg benzoic acid/kg body weight in mice (McCormick, 1974; Abe et al., 1984), the acute toxicity of benzoic acid is low. Clinical signs of intoxication (reported for rats only) included diarrhoea, muscular weakness, tremors, hypoactivity, and entaciation (Bio-Fax, 1973). With oral LD_{50} values of 2100-4070 mg sodium benzoate/kg body weight in rats, the acute toxicity of sodium benzoate is similar to that of benzoic acid, as are the symptoms (Smyth & Carpenter, 1948; Deuel et al., 1954; Bayer AG, 1977)." (as cited in WHO 2000).

With similar metabolism to mammals, and with the known low toxicity of benzoic acid to mammals, there is no reason to anticipate that this compound would be more toxic to birds. In fact, benzoic acid often is added as a preservative to poultry feed at levels not exceeding 0.1%. The acute toxicity to birds is expected to be similar to that in mammals, or approximately at the limit dose required in OPPTS 870.2100.

Conclusion
On the basis of the above, it can be reliably concluded that benzoic acid will be of a low order of acute toxicity to avian species. Birds such as would be used in conducting a study (either Northern bobwhite, *Colinus virginianus* (L.), or mallard, *Anas platyrhynchos* L.) are exposed to high environmental levels of benzoic acid, with no known adverse effects ever having been reported. Benzoic acid can be considered to present little hazard to avian species from the proposed use of MICROL Preservative.

References: (full reports are included in Petro-Canada Report MICROL-2004-03)

WORLD HEALTH ORGANIZATION. 2000. CONCISE INTERNATIONAL. CHEMICAL ASSESSMENT DOCUMENT NO. 26. ENZOIC ACID AND SODIUM BENZOATE

WORLD HEALTH ORGANIZATION. 1996. BENZYL ACETATE, BENZYL ALCOHOL, BENZALDEHYDE, AND BENZOIC ACID AND ITS SALTS. TOXICOLOGICAL EVALUATION OF CERTAIN FOOD ADDITIVES. Prepared by the 46th meeting of the Joint FAO/WHO Expert Committee on Food Additives (JEFCA). WHO Food Additives Series 37

NIOSH. 2004. RTECS Database for Benzoic Acid

Title

MICROL Preservative: Request for Waivers

Data Requirements

OPPTS 850.2100 Avian acute toxicity

Author

E. A. Brown
ChemReg International, LLC
1990 Old Bridge Road, Suite 201
Lake Ridge, VA 20192

Sponsor

Petro-Canada
Specialty Products and Fluids
2489 North Sheridan Way
Mississauga, Ontario Canada L5K 1A8

Study Completion Date

December 2, 2004

Report Number

MICROL-2004-05

Total pages: 6

Statement of Data Confidentiality Claim

No information is claimed confidential on the basis of its falling within the scope of FIFRA § 10(d)(1)(A), (B), or (C).

Company: Petro-Canada
Specialty Products and Fluids

Submitter Name: Elizabeth Anne Brown
ChemReg International, LLC
Authorized Agent for Petro-Canada

Signed: Elizabeth Anne Brown

Date: December 2, 2004

Good Laboratory Practices Statement

The submitter of this study was neither the sponsor of this study nor conducted it, and does not know whether it has been conducted in accordance with 40 CFR Part 160.

Author
Submitter: Elizabeth Anne Brown Date: Dec 2, 2004

Elizabeth Anne Brown
ChemReg International, LLC

OPPTS 850.2100 Avian Acute Toxicity

A from the requirement to conduct a study to determine the acute toxicity of MICROL Preservative is requested. MICROL Preservative is 100% USP grade benzoic acid, an extremely well-known direct food additive and preservative. The proposed use is indoor, nonfood, as an antimicrobial additive to lubricating oils used in food processing equipment. While it and the very closely related sodium benzoate have been extensively researched and are ubiquitous in nature, there are no known studies to determine the acute oral toxicity of either compound to birds. However, there are adequate bases for determining that such a study can be waived without unreasonable adverse effect.

Natural occurrence of Benzoic Acid: (as cited from WHO 2000)

"Benzoic acid is produced by many plants as an intermediate in the formation of other compounds (Goodwin, 1976). High concentrations are found in certain berries.... Benzoic acid has also been detected in animals (see section 6.1). Benzoic acid therefore occurs naturally in many foods, including milk products (Sieber et al., 1989, 1990)."

"Generally, benzoic acid can occur in almost all environmental compartments. Whether it exists in the undissociated or dissociated form depends on the specific physicochemical conditions. Above pH 6, the benzoate anion prevails (Chipley, 1983)."

"Benzoic acid occurs naturally in free and bound form in many plant and animal species. It is a common metabolite in plants and organisms (Hegnauer, 1992). Appreciable amounts have been found in gum benzoin (around 20%) and most berries (around 0.05%) (Budavari et al., 1996). For example, ripe fruits of several *Vaccinium* species (e.g., cranberry, *V. vitis idaea*; bilberry, *V. macrocarpon)* contain as much as 300-1300 mg free benzoic acid per kg fruit (Hegnauer, 1966). Benzoic acid is also formed in apples after infection with the fungus *Nectria galligena* (Harborne, 1983) or in *Pinus thunbergii* callus inoculated with a pathogenic pine wood nematode *(Bursaphelenchus xylophilus)* (Zhang et al., 1997). Among animals, benzoic acid has been identified primarily in omnivorous or phytophageous species, e.g., in viscera and muscles of the ptarmigan *(Lagopus mutus)* (Hegnauer, 1989) as well as in gland secretions of male muskoxen *(Ovibos moschatus)* (Flood et al., 1989) or Asian bull elephants *(Elephas maximus)* (Rasmussen et al., 1990)."

"Owing to its occurrence in many organisms, benzoic acid is naturally present in foods (review in Sieber et al., 1989, 1990). Some typical examples specifying reported ranges of means in selected foods have been compiled from Sieber et al. (1989) as follows:

Milk	traces - 6 mg/kg
Yoghurt	12-40 mg/kg
Cheese	traces - 40 mg/kg
Fruits (excluding *Vaccinium* species)	traces - 14 mg/kg
Potatoes, beans, cereals	traces - 0.2 mg/kg
Soya flour, nuts	1.2-11 mg/kg

"Honeys from different floral sources (n = 7) were found to contain free benzoic acid at concentrations of <10 mg/kg (n = 5) and of <100 mg/kg (n = 2) (Steeg & Montag, 1987)."

Acute toxicity of Benzoic Acid to Mammals and Relation to Birds

"After oral uptake, benzoic acid and sodium benzoate are rapidly absorbed from the gastrointestinal tract and metabolized in the liver by conjugation with glycine, resulting in the formation of hippuric acid, which is rapidly excreted via the urine. To a lesser extent, benzoates applied dermally can penetrate through the skin. Owing to rapid metabolism and excretion, an accumulation of the benzoates or their metabolites is not to be expected." (WHO 2000)

"In the acid conditions of the stomach, the equilibrium moves to the undissociated benzoic acid molecule, which should be absorbed rapidly. Benzoate from sodium benzoate would change from the ionized form to the undissociated benzoic acid molecule. As a result, the metabolism and systemic effects of benzoic acid and sodium benzoate can be evaluated together." (WHO 2000)

WHO 1996 reports that birds metabolize benzoic acid acid and sodium benzoate in a similar manner to man and other mammal, with rapid excretion primarily as hippuric acid.

The acute oral LD50 of benzoic acid to rats is 2000-2500 mg/kg bw (Ignat'ev (1965), as cited in WHO 1996). According to the RTECS Database for Benzoic acid (RTECS # DG0875000), the acute oral LD50 in rats is 1,700 mg/kg bw (as cited by NIOSH, 2004).

"With oral LD_{50} values (administration by gavage) of 3040 mg benzoic acid/kg body weight in rats (Bio-Fax, 1973) and 1940-2263 mg benzoic acid/kg body weight in mice (McCormick, 1974; Abe et al., 1984), the acute toxicity of benzoic acid is low. Clinical signs of intoxication (reported for rats only) included diarrhoea, muscular weakness, tremors, hypoactivity, and emaciation (Bio-Fax, 1973). With oral LD_{50} values of 2100-4070 mg sodium benzoate/kg body weight in rats, the acute toxicity of sodium benzoate is similar to that of benzoic acid, as are the symptoms (Smyth & Carpenter, 1948; Deuel et al., 1954; Bayer AG, 1977)." (as cited in WHO 2000).

With similar metabolism to mammals, and with the known low toxicity of benzoic acid to mammals, there is no reason to anticipate that this compound would be more toxic to birds. In fact, benzoic acid often is added as a preservative to poultry feed at levels not exceeding 0.1%. The acute toxicity to birds is expected to be similar to that in mammals, or approximately at the limit dose required in OPPTS 870.2100.

Conclusion
On the basis of the above, it can be reliably concluded that benzoic acid will be of a low order of acute toxicity to avian species. Birds such as would be used in conducting a study (either Northern bobwhite, *Colinus virginianus* (L.), or mallard, *Anas platyrhynchos* L.) are exposed to high environmental levels of benzoic acid, with no known adverse effects ever having been reported. Benzoic acid can be considered to present little hazard to avian species from the proposed use of MICROL Preservative.

References: (full reports are included in Petro-Canada Report MICROL-2004-03)

WORLD HEALTH ORGANIZATION. 2000. CONCISE INTERNATIONAL CHEMICAL ASSESSMENT DOCUMENT NO. 26. ENZOIC ACID AND SODIUM BENZOATE

WORLD HEALTH ORGANIZATION. 1996. BENZYL ACETATE, BENZYL ALCOHOL, BENZALDEHYDE, AND BENZOIC ACID AND ITS SALTS. TOXICOLOGICAL EVALUATION OF CERTAIN FOOD ADDITIVES. Prepared by the 46th meeting of the Joint FAO/WHO Expert Committee on Food Additives (JEFCA). WHO Food Additives Series 37

NIOSH. 2004. RTECS Database for Benzoic Acid

Title

MICROL Preservative: Request for Waivers

Data Requirements

OPPTS 835.2120 - Hydrolysis

Author

E. A. Brown
ChemReg International, LLC
1990 Old Bridge Road, Suite 201
Lake Ridge, VA 20192

Sponsor

Petro-Canada
Specialty Products and Fluids
2489 North Sheridan Way
Mississauga, Ontario Canada L5K 1A8

Study Completion Date

December 2, 2004

Report Number

MICROL-2004-06

Total pages: 4

Statement of Data Confidentiality Claim

No information is claimed confidential on the basis of its falling within the scope of FIFRA § 10(d)(1)(A), (B), or (C).

Company: Petro-Canada
Specialty Products and Fluids

Submitter Name: Elizabeth Anne Brown
ChemReg International, LLC
Authorized Agent for Petro-Canada

Signed: Elizabeth Anne Brown

Date: December 2, 2004

Good Laboratory Practices Statement

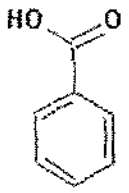
The submitter of this study was neither the sponsor of this study nor conducted it, and does not know whether it has been conducted in accordance with 40 CFR Part 160.

Author
Submitter: Elizabeth Anne Brown Date: Dec 2, 2004

Elizabeth Anne Brown
ChemReg International, LLC

A waiver from the requirement to conduct a study to fulfill OPPTS 835.2120 (EPA Guideline 161-1) is requested on the basis that the active ingredient is a well-known chemical that is not subject to hydrolysis

The active ingredient in MICROL Preservative is Benzoic Acid (CAS 65-85-0), with the following structure:



Benzoic acid is a well-known carboxylic acid, with a pKa of 4.19. It is expected to be stable to hydrolysis at pH in the ranges of 5-9, based on its chemical structure and based on known hydrolytic mechanisms.

Reference:

Lyman, W.J., W. F. Reehl, D.H. Rosenblatt. 1990. Handbook of chemical property estimation methods. Environmental behavior of organic compounds. American Chemical Society, Washington. DC. (Chapter 7).

Title

MICROL Preservative: Request for Waivers

Data Requirements

OPPTS 835.2120 - Hydrolysis

Author

E. A. Brown
ChemReg International, LLC
1990 Old Bridge Road, Suite 201
Lake Ridge, VA 20192

Sponsor

Petro-Canada
Specialty Products and Fluids
2489 North Sheridan Way
Mississauga, Ontario Canada L5K 1A8

Study Completion Date

December 2, 2004

Report Number

MICROL-2004-06

Total pages: 4

Statement of Data Confidentiality Claim

No information is claimed confidential on the basis of its falling within the scope of FIFRA § 10(d)(1)(A), (B), or (C).

Company: Petro-Canada
Specialty Products and Fluids

Submitter Name: Elizabeth Anne Brown
ChemReg International, LLC
Authorized Agent for Petro-Canada

Signed: Elizabeth Anne Brown

Date: December 2, 2004

Good Laboratory Practices Statement

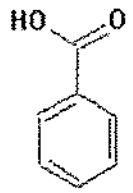
The submitter of this study was neither the sponsor of this study nor conducted it, and does not know whether it has been conducted in accordance with 40 CFR Part 160.

Author
Submitter: Elizabeth Anne Brown Date: Dec 2, 2004

Elizabeth Anne Brown
ChemReg International, LLC

A waiver from the requirement to conduct a study to fulfill OPPTS 835.2120 (EPA Guideline 161-1) is requested on the basis that the active ingredient is a well-known chemical that is not subject to hydrolysis

The active ingredient in MICROL Preservative is Benzoic Acid (CAS 65-85-0), with the following structure:



Benzoic acid is a well-known carboxylic acid, with a pKa of 4.19. It is expected to be stable to hydrolysis at pH in the ranges of 5-9, based on its chemical structure and based on known hydrolytic mechanisms.

Reference:

Lyman, W.J., W. F. Reehl, D.H. Rosenblatt. 1990. Handbook of chemical property estimation methods. Environmental behavior of organic compounds. American Chemical Society, Washington. DC. (Chapter 7).

Title

MICROL Preservative: Request for Waivers

Data Requirements

OPPTS 835.2120 - Hydrolysis

Author

E. A. Brown
ChemReg International, LLC
1990 Old Bridge Road, Suite 201
Lake Ridge, VA 20192

Sponsor

Petro-Canada
Specialty Products and Fluids
2489 North Sheridan Way
Mississauga, Ontario Canada L5K 1A8

Study Completion Date

December 2, 2004

Report Number

MICROL-2004-06

Total pages: 4

Statement of Data Confidentiality Claim

No information is claimed confidential on the basis of its falling within the scope of FIFRA § 10(d)(1)(A), (B), or (C).

Company: Petro-Canada
Specialty Products and Fluids

Submitter Name: Elizabeth Anne Brown
ChemReg International, LLC
Authorized Agent for Petro-Canada

Signed: Elizabeth Anne Brown

Date: December 2, 2004

Good Laboratory Practices Statement

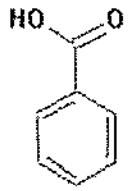
The submitter of this study was neither the sponsor of this study nor conducted it, and does not know whether it has been conducted in accordance with 40 CFR Part 160.

Author
Submitter: Elizabeth Anne Brown Date: Dec 2, 2004

Elizabeth Anne Brown
ChemReg International, LLC

A waiver from the requirement to conduct a study to fulfill OPPTS 835.2120 (EPA Guideline 161-1) is requested on the basis that the active ingredient is a well-known chemical that is not subject to hydrolysis

The active ingredient in MICROL Preservative is Benzoic Acid (CAS 65-85-0), with the following structure:



Benzoic acid is a well-known carboxylic acid, with a pKa of 4.19. It is expected to be stable to hydrolysis at pH in the ranges of 5-9, based on its chemical structure and based on known hydrolytic mechanisms.

Reference:

Lyman, W.J., W. F. Reehl, D.H. Rosenblatt. 1990. Handbook of chemical property estimation methods. Environmental behavior of organic compounds. American Chemical Society, Washington, DC. (Chapter 7).

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

December 20, 2004

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

PLEASE RETURN A COPY OF THIS LETTER WITH PAYMENT

OPP Decision Number: D-352089
EPA File Symbol or Registration Number: 82076-R
Product Name: MICROL PRESERVATIVE
EPA Receipt Date: 16-Dec-2004
EPA Company Number: 82076
Company Name: PETRO-CANADA

ELIZABETH ANNE BROWN
CHEMREG INTERNATIONAL LLC
PETRO-CANADA
1990 OLD BRIDGE ROAD, SUITE 201
LAKE RIDGE, VA 22191-2383

SUBJECT: Receipt of Registration Application Subject to Registration Service Fee

Dear Registrant:

The Office of Pesticide Programs has received your application for registration. If you submitted data with this application, the results of the PRN-86-5 screen will be communicated separately. During the administrative screen, the Office of Pesticide Programs has determined that this Action is subject to a Pesticide Registration Service Fee as defined in the Pesticide Registration Improvement Act.

The Action has been identified as Action Code: A38

NEW AI;FOOD USE;WITH EXEMPTION;

Please remit payment in the amount of: $ 90,000 to:

By USPS:
USEPA Washington Finance Center
Pesticide Registration Service Fee
PO Box 360277
Pittsburgh, PA 15251

By Courier:
U.S. EPA Washington Finance Center
Pesticide Registration Service Fee
C/O Mellon Client Service Center
500 Ross Street, Room 670
Box 360277
Pittsburgh, PA 15251-6277
Attn: EPA Module Supervisor
Telephone: (412) 236-2294

All payments must be in United States currency by check, bank draft, or money order drawn to the order of the Environmental Protection Agency. To ensure proper credit, please write the OPP DECISION NUMBER on your check, and enclose a copy of this letter with your payment.

You may be eligible for a full or partial waiver of the registration service fee if, for example, you qualify as a small business or are applying for a minor use, or if your application is solely associated with an IR-4 tolerance petition. Please be advised that if you intend to request a waiver, you must do so in writing within 15 days of receipt of this invoice instead of remitting the amount indicated above. OPP will not consider waiver requests after the registration service fee has been paid. Information regarding eligibility and how th request and document a fee waiver is available on the OPP Fee for Service web site at www.epa.gov/pesticides/fees.

If you have any questions, please contact the Pesticide Registration Service Fee Ombudsman at (703) 308-6432.

Sincerely,

Front End Processing Staff
Information Resources and Services Division

ChemReg
INTERNATIONAL, LLC

464641-00

1990 OLD BRIDGE ROAD, SUITE 201
LAKE RIDGE, VIRGINIA 22192-2383

DIRECT: 703-492-7905
MAIN: 703-492-0445
FAX: 703-492-0668

E-MAIL: brown@chemreg.com
WEB SITES: www.chemreg.com
www.pesticide.net

ELIZABETH A. BROWN, PH.D.

December 16, 2004

Document Processing Desk (APPL, REGFEE, NEWCO, COADR)
U.S. Environmental Protection Agency (7505C)
Office of Pesticide Programs
Room 266A, Crystal Mall 2
1801 South Bell Street
Arlington, VA 22202-4501

Attn: Velma Noble (PM 31)

Re: Application for Registration of MICROL Preservative
Request for Company Number

Dear Velma:

On behalf of our client, Petro-Canada, Specialty Products and Fluids (Petro-Canada), enclosed please find an application for registration of MICROL Preservative, which contains a new antimicrobial active ingredient.

This application has been previously discussed with the Agency, including discussion on June 5, 2003 for the required approach and multiple discussions and communications during February through May 2004.

This application is subject to PRIA. We believe, based on conversations with Mr. Dennis Edwards, that this application is Fee Category A38, with the associated fee of $90,000. . Please contact me directly at 703-492-7905 or brown@chemreg.com, if there any questions regarding the PRIA category.

Enclosed with this application, please find the following:

1. EPA Form 8570-1
2. EPA Form 8570-34, Certification with respect to citation of data
3. EPA Form 8570-35, Data matrix (Agency Use and Public File copies)
4. EPA Form 8570-4, Confidential Statement of Formula
5. A letter from Petro-Canada, requesting a new company number and assigning ChemReg International, LLC, as their US agent
6. Five (5) copies of the proposed labeling
7. Transmittal bibliography
8. Three (3) copies of each submitted study)

If there are any questions or if anything further is needed, please do not hesitate to contact me directly. Please keep me informed of the progress of this application.

Regards,

Elizabeth Anne Brown

Elizabeth Anne Brown

cc: Petro-Canada, Specialty Products and Fluids

TRANSMITTAL DOCUMENT

Submitter
Petro-Canada
Specialty Product and Fluids
2489 North Sheridan Way
Mississauga, Ontario L5K 1A8 CANADA

Regulatory action in support of which this package is submitted
New Product Registration (New Antimicrobial Active Ingredient
(MICROL Preservative, no company number yet assigned)

Transmittal Date
December 16, 2004, 2004

Submitted Studies

	MRID	
----		Administrative Materials
Document 1:	46464101	Brown, E.A. Dec 14, 2004. MICROL Preservative. Product Identity, Composition, and Analysis (Group A). Report No. MICROL-2004-01. ChemReg International, LLC. 77 pages. Contains Business Confidential Information
Document 2:	46432702	Brown, E.A. November 22, 2004. MICROL Preservative. Physical and Chemical Properties (Group B). Report No. MICROL-2004-02. ChemReg International, LLC. 43 pages
Document 3:	46432703	Brown, E.A. December 6, 2004. MICROL Preservative. Toxicology. Report No. MICROL-2004-03. ChemReg International, LLC. 225 pages.
Document 4	46432704	Brown, E.A. Dec 2, 2004. MICROL Preservative. Ecotoxicology. Report No. MICROL-2004-04. ChemReg International, LLC. 52 pages.
Document 5	46432705	Brown, E.A. December 2, 2004. MICROL Preservative. Request for Waivers – Ecotoxicology. ChemReg International, LLC. 6 pages.
Document 6	46432706	Brown, E.A. December 2, 2004. MICROL Preservative. Request for Waivers – Hydrolysis. ChemReg International, LLC. 4 pages

Company Official: Elizabeth Anne Brown

Company Name: ChemReg International, LLC., Authorized Agent for Buzz Off Insect Shield

Company Contact: Elizabeth Anne Brown

Phone Number: 703-492-7905

ChemReg
INTERNATIONAL, LLC

1990 OLD BRIDGE ROAD, SUITE 201
LAKE RIDGE, VIRGINIA 22192-2383

DIRECT: 703-492-7905
MAIN: 703-492-0445
FAX: 703-492-0668

E-MAIL: brown@chemreg.com
WEB SITES: www.chemreg.com
www.pesticide.net

ELIZABETH A. BROWN, PH.D.

82076
12/17/04

December 16, 2004

Document Processing Desk (APPL, REGFEE, NEWCO, COADR)
U.S. Environmental Protection Agency (7505C)
Office of Pesticide Programs
Room 266A, Crystal Mall 2
1801 South Bell Street
Arlington, VA 22202-4501

Attn: Velma Noble (PM 31)

Re: Application for Registration of MICROL Preservative
Request for Company Number

Dear Velma:

On behalf of our client, Petro-Canada, Specialty Products and Fluids (Petro-Canada), enclosed please find an application for registration of MICROL Preservative, which contains a new antimicrobial active ingredient.

This application has been previously discussed with the Agency, including discussion on June 5, 2003 for the required approach and multiple discussions and communications during February through May 2004.

This application is subject to PRIA. We believe, based on conversations with Mr. Dennis Edwards, that this application is Fee Category A38, with the associated fee of $90,000. . Please contact me directly at 703-492-7905 or brown@chemreg.com if there any questions regarding the PRIA category.

Enclosed with this application, please find the following:

1. EPA Form 8570-1
2. EPA Form 8570-34, Certification with respect to citation of data
3. EPA Form 8570-35, Data matrix (Agency Use and Public File copies)
4. EPA Form 8570-4, Confidential Statement of Formula
5. A letter from Petro-Canada, requesting a new company number and assigning ChemReg International, LLC, as their US agent
6. Five (5) copies of the proposed labeling
7. Transmittal bibliography
8. Three (3) copies of each submitted study)

If there are any questions or if anything further is needed, please do not hesitate to contact me directly. Please keep me informed of the progress of this application.

Regards,

Elizabeth Anne Brown

Elizabeth Anne Brown

cc: Petro-Canada, Specialty Products and Fluids

TRANSMITTAL DOCUMENT

Submitter
Petro-Canada
Specialty Product and Fluids
2489 North Sheridan Way
Mississauga, Ontario L5K 1A8 CANADA

Regulatory action in support of which this package is submitted
New Product Registration (New Antimicrobial Active Ingredient
(MICROL Preservative, no company number yet assigned)

Transmittal Date
December 16, 2004, 2004

Submitted Studies

	MRID	
---		Administrative Materials
Document 1:		Brown, E.A. Dec 14, 2004. MICROL Preservative. Product Identity, Composition, and Analysis (Group A). Report No. MICROL-2004-01. ChemReg International, LLC. 77 pages. Contains Business Confidential Information
Document 2:		Brown, E.A. November 22, 2004. MICROL Preservative. Physical and Chemical Properties (Group B). Report No. MICROL-2004-02. ChemReg International, LLC. 43 pages.
Document 3:		Brown, E.A. December 6, 2004. MICROL Preservative. Toxicology. Report No. MICROL-2004-03. ChemReg International, LLC. 225 pages.
Document 4		Brown, E.A. Dec 2, 2004. MICROL Preservative. Ecotoxicology. Report No. MICROL-2004-04. ChemReg International, LLC. 52 pages.
Document 5		Brown, E.A. December 2, 2004. MICROL Preservative. Request for Waivers – Ecotoxicology. ChemReg International, LLC. 6 pages.
Document 6		Brown, E.A. December 2, 2004. MICROL Preservative. Request for Waivers – Hydrolysis. ChemReg International, LLC. 4 pages

Company Official: Elizabeth Anne Brown

Company Name: ChemReg International, LLC., Authorized Agent for Buzz Off Insect Shield

Company Contact: Elizabeth Anne Brown

Phone Number: 703-492-7905

Pre application Discussion

Jack Housenger/DC/USEPA/US
10/25/2004 09:02 AM

To Andrew Simons/DC/USEPA/US@EPA, Dennis Edwards/DC/USEPA/US@EPA, Marshall Swindell/DC/USEPA/US@EPA, hardy.michael@epa.gov,
cc
bcc
Subject Fw: background for minor use waiver discussion

for our meeting tomorrow

Jack E. Housenger, Associate Director
Antimicrobials Division
Office of Pesticide Programs
703-308-8163
Visit: http://www.epa.gov/pesticides/
----- Forwarded by Jack Housenger/DC/USEPA/US on 10/25/2004 09:04 AM -----

Elizabeth Brown <brown@chemreg.com>
10/22/2004 12:19 PM

To Jack Housenger/DC/USEPA/US@EPA
cc
Subject background for minor use waiver discussion

Benzoic Acid

file

look for my notes on this meeting!!

Jack:
As requested, here's the background for our meeting on Tuesday, Oct 26 at 2:00 pm, for whether an antimicrobial can qualify for reduction or full waiver of application fees under the minor use provisions. I will provide specific information about the potential application that has raised the question when we meet.

The attached are a letter with my thinking on the basis, as well as a referenced FR citation.
Looking forward to Tuesday!
Elizabeth
<<20041022.ltr to Housenger.minor use waiver background.doc>> <<Pages from 64FR 50671 Antimicrobial reg req draft rule.pdf>>

Elizabeth Anne Brown, Ph.D.
Director, Scientific & Regulatory Affairs
ChemReg International
1990 Old Bridge Road, Suite 201
Lake Ridge, VA 22192

Phone: 703-492-7905
Fax: 703-492-0668
Email: brown@chemreg.com



20041022.ltr to Housenger.minor use waiver background.doc Pages from 64FR 50671 Antimicrobial reg req draft rule.pdf

10/25/04

Pre-Meeting on Minor Use Waivers for PRIA fees

EPA (Andy Simons, Rick Kegwin, Phil Ross, Dennis Edwards, Tracy Lantz, Jack Housenger, Marshall Swindell)

Discussion in Jack's office prior to meeting with Elizabeth Brown.
We think the product she is interested in a lubricating oil with only one user.

Congress did not decide to give blanket fee waivers for antimicrobials.

Does Elizabeth think that antimicrobials do not have to meet the definition of 2 (ll)?
Her product does not make public health claims

Meeting with Elizabeth Brown of ChemReg on Minor Use Waivers for PRIA fees

In addition to the above mentioned individuals. Michael Hardy also joined the meeting.

Meeting was held in 308U.

The product she is interested in registering is Benzoic Acid
It is for use as an additive/lubricant for food processing equipment, is a GRAS additive, 4 (B) inert, but no longer registered with the EPA as an AI.

No interested in public health claims, only want to say that it prevents degradation of the oil, the lubricant would be a treated article.

The company she is representing is not a small business (Petro Canada).

Dennis-this would fall into the New AI food use category $90,000 PRIA fee

Elizabeth-[redacted]
Can this be classified as a minor use?

Jack-her product doesn't meet the 2 (ll) definition.

Phil-for waiver product would have to meet the definition of a minor use, in such that these is not sufficient economic incentive to register the product.

Jack-can she get reduced fees? Some of the reviews have already been done in support of another applicant

Elizabeth-her product reduces cross contamination

EPA-we don't consider this a public health claim

Elizabeth-they could license product to another company and then buy it back from that company.

EPA-this brings about concerns as to whether this business has been formed or manipulated to avoid paying the fee? via a licensing agreement.
We would know that the other company has been manipulated.

Phil-limited licensing or partnering may be OK

Or maybe she could use a different AI (Na Benzoit) that is already registered by would be a new food use-fee $10,000

Andy Simmons Dennis Edwards
Rick Keigwin Jack Housenger
Phil Ross Tracy Lantz
Marshall

Pre Meeting 10/25/04
Minor Use Waivers for PRIA fees

We think this is for some sort of lubricating oil with only one user.

Congress did not decide to give fee waivers for antimicrobials

does she think that an antimicrobial does not have to meet the definition of 2(11)
her product ~~[illegible]~~ is not a public health product

Michael Hardy Meeting w/ Elizabeth Brown

Elizabeth Brown

Minor Uses for Antimicrobials
Benzoic acid — for use as additive to lubricants for food processing equip.
GRAS food additive
4 B inert
no longer EPA AI

claim prevents degredation of oil
(No public health claim)
the lubricant would be a treated article

this Company is not a small business
Dennis new AI food use category $90,000 PRIA fee

[redacted]

Elizabeth can this be classified as a minor use?

Jack – she doesn't meet 2 (LL) definition.

Phil – have to be a minor use and not provide sufficient economic incentive

Jack – can she reduce fees? if reviews have already been done is support of another application

She says it reduces cross contamination — we don't consider a public health claim.

Elizabeth they could license product to another co. then buy it back.

has the business been formed or manipulated to avoid paying fee? licensing agreement

we would know that the other company has been manipulated

Phil – limited licensing or partnering > maybe ok

Na Benzoit

or may use a different AI already registered but would be new food use — $10,000

ChemReg
INTERNATIONAL, LLC

1990 OLD BRIDGE ROAD, SUITE 201
LAKE RIDGE, VIRGINIA 22192-2383

DIRECT: 703-492-7905
MAIN: 703-492-0445
FAX: 703-492-0668

E-MAIL: hrown@chemreg.com
WEB SITES: www.chemreg.com
www.pesticide.net

ELIZABETH A. BROWN, PH.D.

Via Email

October 22, 2004

Dr. Jack Housenger
US-EPA/OPP/AD
1801 South Bell Street
Arlington, VA 22202-4501

Dear Jack:

As requested, the following is background pertinent to our meeting on Tuesday, October 26, 2004 at 2:00 pm to discuss the circumstances under which an antimicrobial pesticide product might qualify for waiver of PRIA applications fees under the minor use provisions. These are my thoughts on the basis for a minor use waiver, but these certainly are not meant to be all-encompassing. Historically, "minor use" has been associated with agricultural uses of pesticides via the IR-4 program, but FIFRA identifies other bases for minor use determination.

FIFRA 33(b)(7) identifies where PRIA application fees may be reduced or waived, assuming appropriate documentation is included. There are four circumstances identified in FIFRA 33(b)(7)(D) through (G) as basis for reduction or waiver of fees. The exact wording in (E) and (G) of FIFRA follows:

> (D) MINOR USES. -
>
> > (i) IN GENERAL. The Administrator may waive or reduce a registration service fee for an application for minor uses for a pesticide.
> > (ii) SUPPORTING DOCUMENTATION. - An applicant requesting a waiver under this subparagraph shall provide supporting documentation that demonstrates, anticipated revenues from the uses that are the subject of the application would be insufficient to justify to the satisfaction of the Administrator, that imposition of

the full application fee.

(E) IR-4 WAIVER. - The Administrator shall waive the registration service fee for an application if the Administrator determines that –

(i) the application is solely associated with a tolerance petition submitted in connection with the Inter-Regional Project Number 4 (IR-4) as described in section 2 of Public Law 89-106 (7 U.S.C. 450i(e)); and
(ii) the waiver is in the public interest.

It is important to note the wording associated with (D) – that "anticipated revenues would be insufficient to justify …imposition of the full application fee." There is no further requirement or condition associated with that definition of "minor use" for reduction or waiver of the PRIA application fee.

The term "minor use" occurs elsewhere within FIFRA, with inconsistent definition. It is important to separate out where the definition is appropriate to consideration of a waiver under PRIA.

FQPA

FIFRA Section 2 (ll) defines minor use in the following manner, which is the historical interpretation as associated with the more typical agricultural uses, requiring in all cases consultation with the Secretary of Agriculture:

Minor Use. -- The term "minor use" means the use of a pesticide on an animal, on a commercial agricultural crop or site, or for the protection of public health ← where--

(1) the total United States acreage for the crop is less than 300,000 acres, as determined by the Secretary of Agriculture; or
(2) the Administrator, in consultation with the Secretary of Agriculture, determines that, based on information provided by an applicant for registration or a registrant, the use does not provide sufficient economic incentive to support the initial registration or continuing registration of a pesticide for such use and- (meets the following one of the following

many of our products may fall into this definition and qualify for waivers

(A) there are insufficient efficacious alternative registered pesticides available for the use;
(B) the alternatives to the pesticide use pose greater risks to the environment or human health;
(C) the minor use pesticide plays or will play a significant part in managing pest resistance; or
(D) the minor use pesticide plays or will play a significant part in an integrated pest management program.

> The status as a minor use under this subsection shall continue as long as the Administrator has not determined that, based on existing data, such use may cause an unreasonable adverse effect on the environment and the use otherwise qualifies for such status.

However, FIFRA Section 4 (i)(4) actually provides several different definitions of a minor use. Even though the fees under this section of FIFRA are not currently in force because of PRIA, the definition and explanation are clearly pertinent to the similar situation for fees under PRIA. The following is the exact wording of that section (emphasis added):

> (4) Reduction or Waiver of Fees for Minor Use and Other Pesticides. --
>
> (A) An active ingredient that is contained only in pesticides that are registered solely for agricultural or nonagricultural minor uses, or a pesticide the value or volume of use of which is small, shall be exempt from the fees prescribed by paragraph (3).
>
> (B) The Administrator shall exempt any public health pesticide from the payment of the fee prescribed under paragraph (3) if, in consultation with the Secretary of Health and Human Services, the Administrator determines, based on information supplied by the registrant, that the economic return to the registrant from sales of the pesticide does not support the registration or reregistration of the pesticide.
>
> ***(C) An antimicrobial active ingredient, the production level of which does not exceed 1,000,000 pounds per year, shall be exempt from the fees prescribed by paragraph (3). For purposes of this subparagraph, the term "antimicrobial active ingredient' means any active ingredient that is contained only in pesticides that are not registered for any food or feed use and that are--***
>
> ***(i) sanitizers intended to reduce the number of living bacteria or viable virus particles on inanimate surface or in water or air;***
>
> ***(ii) bacteriostats intended to inhibit the growth of bacteria in the presence of moisture;***
>
> ***(iii) disinfectants intended to destroy or irreversibly inactivate bacteria, fungi, or viruses on surfaces or inanimate objects;***
>
> ***(iv) sterilizers intended to destroy viruses and all living bacteria, fungi, and their spores on inanimate surfaces; or***
>
> ***(v) fungicides or fungistats.***
>
> (D)(i) Notwithstanding any other provision of this subsection, in the case of a small business registrant of a pesticide, the registrant shall pay a fee for the reregistration of each active ingredient of the pesticide that does not exceed an amount determined in accordance with this subparagraph.
>
> (ii) If during the 3-year period prior to reregistration the average annual gross revenue of the registrant from pesticides containing such active ingredient is--

(I) less than $5,000,000, the registrant shall pay 0.5 percent of such revenue;
(II) $5,000,000 or more but less than $10,000,000, the registrant shall pay 1 percent of such revenue; or
(III) $10,000,000 or more, the registrant shall pay 1.5 percent of such revenue, but not more than $ 150,000.

(iii) For the purpose of this subparagraph, a small business registrant is a corporation, partnership, or unincorporated business that--
(I) has 150 or fewer employees; and
(II) during the 3-year period prior to reregistration, had an average annual gross revenue from chemicals that did not exceed $40,000,000.

The definition of "antimicrobial pesticide" also is important, as well as the Agency's prior guidance on that definition. FIFRA Section 2(mm) defines an antimicrobial pesticide as:

(1) In General. -- The term "antimicrobial pesticide" means a pesticide that--
(A) is intended to--
(i) disinfect, sanitize, reduce, or mitigate growth or development of microbiological organisms; or
(ii) protect inanimate objects, industrial processes or systems, surfaces, water, or other chemical substances from contamination, fouling, or deterioration caused by bacteria, viruses, fungi, protozoa, algae, or slime; and
(B) in the intended use is exempt from, or otherwise not subject to, a tolerance under section 408 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 346a and 348) or a food additive regulation under section 409 of such Act.
(2) Excluded Products. -- The term "antimicrobial pesticide" does not include --
(A) a wood preservative or antifouling paint product for which a claim of pesticidal activity other than or in addition to an activity described in paragraph (1) is made;
(B) an agricultural fungicide product; or
(C) an aquatic herbicide product.
(3) Included Products. -- The term "antimicrobial pesticide" does include any other chemical sterilant product (other than liquid chemical sterilant products exempt under subsection (tt)), any other disinfectant product, any other industrial microbiocide product, and any other preservative product that is not excluded by paragraph (2).

In proposed rulemaking published in the Federal Register on September 17, 1999 (64 FR 50671) for antimicrobial pesticides, the Agency clearly articulated its position regarding what is and is not "food" use as associated with FIFRA 2(mm)(1)(B) on pages 50677-78 (Section IV). That interpretation, even though never issued as a final rule, has been used by the Agency since

that time in various decisions and has been publicly reiterated by key Agency personnel on multiple occasions. That guidance (attached as a pdf file) states: "An antimicrobial pesticide, then, is a product bearing only non-food uses, only food uses covered by an existing clearance under FFDCA, or some combination of these two." Those antimicrobial pesticides (or uses thereof) which do not require establishment of, increase in, or exemption from tolerance as a new regulation thus remain within the definition of "antimicrobial pesticide" for the purposes of FIFRA(mm)(1)(B).

Preliminary guidance on fee waivers published by EPA on its website at http://www.epa.gov/pesticides/fees/questions/waivers.htm#4 refers only to the definition of minor use under FIFRA 2(mm). This preliminary guidance is general across all divisions of OPP. While this likely was driven primarily by the historical definitions and by conventional chemical uses within Registration Division, it fails to take into account the specific wording under FIFRA 33(b)(7)(D) which does not add additional conditions and fails to take into account either Congress's or the Agency's acknowledged special considerations for antimicrobial pesticides.

In conclusion, I believe that there is basis for concluding that an application for an antimicrobial pesticide may be eligible for reduction or waiver of the PRIA application fee strictly on the basis of the potential revenue from the uses contained within that application.

I'll look forward to talking with you on Tuesday. At that time, I'll provide some additional specifics about the potential application for which these issues were raised. I hope you will be able to provide me with some guidance as to the specific documentation which will be needed, if there is agreement that such uses qualify for a reduction/waiver of application fees.

Regards,

Elizabeth Anne Brown

regulations, EPA must address "allocation of appropriate resources to ensure streamlined management of antimicrobial pesticide registrations." The allocation of resources is not a reform that can be accomplished by Agency regulations, and EPA is not proposing any regulations for doing so. Budget and resource allocations are guided by Executive branch and Congressional priorities and are determined year by year based on overall needs of the Agency and the pesticide program.

1. Completeness of Applications

FIFRA section 3(h)(3)(B)(iii)(IV) requires that, in issuing final regulations, EPA must "clarify criteria for determination of the completeness of an application." EPA is today proposing in § 152.3 a definition of a "complete application" for all registration applications. In addition, specific to antimicrobial products, and directly responsive to the requirement of FIFRA section 3(h)(3)(B), EPA is proposing in § 152.450 to describe in detail the contents of an application, and the criteria that will be used to judge the completeness of the application as a whole, and of its individual components. EPA's proposals are discussed further in Unit VIII.F.

V. Other Statutory Provisions Addressed In this Proposal

A. Changes to the Definition of "Pesticide"

FQPA modified FIFRA section 2(u) to exclude certain liquid chemical sterilant products from the definition of "pesticide," and to include certain nitrogen stabilizer products. This provision was effective on August 3, 1996. In recognition of this provision, EPA is proposing to add a new § 152.6 entitled "Substances excluded from regulation by FIFRA." EPA has issued a notice to registrants, entitled "Liquid Chemical Sterilant Products" (PR Notice 98-2; January 15, 1998), explaining how it will treat liquid chemical sterilants affected by section 2(u). Units XIV. and XV. discuss chemical sterilants and nitrogen stabilizers.

B. Notification Procedures

FIFRA section 3(c)(9)(C) now authorizes registrants of antimicrobial products to make certain defined labeling modifications by notification to the Agency instead of amendment, and establishes a procedure for notifications and Agency decisions. This provision was effective on August 3, 1996, and the new procedures are exclusive to antimicrobial products. Today's proposal codifies these new notification procedures. The substance of the expanded notifications permitted by FIFRA section 3(c)(9) is issued in notices to registrants (PR Notices), and not in today's proposal. Unit XVI. discusses antimicrobial notifications.

C. Use Dilution Labeling

FIFRA section 3(c)(9)(D) authorizes registrants to include on their labeling precautionary statements about the product as diluted for use (use dilution labeling). This provision was effective on August 3, 1996. EPA proposes to reformat its human hazard labeling requirements in § 156.10(h) and to incorporate use dilution requirements in appropriate sections. Unit XIII.A. discusses use dilution labeling.

VI. What Is an Antimicrobial Pesticide?

EPA proposes in § 152.3 a definition and interpretation of antimicrobial pesticide. The proposed definition is paraphrased from that in section 2(mm) of FIFRA, and interprets the undefined elements. Because FIFRA section 3(h) directs EPA to develop and implement special procedures in its regulatory program for antimicrobial pesticides, it is important that there be a well-defined and commonly understood universe of products to which the statutory provisions apply. The practical consequences of being included or excluded as an "antimicrobial pesticide" are significant for both pesticide producers and the Agency. FIFRA section 2(mm) defines the term "antimicrobial pesticide," carefully delineating its boundaries to mesh with the practical implementation of section 3(h) requirements. This unit discusses the definition in detail.

A. General Definition

Under FIFRA section 2(mm)(1)(A), an antimicrobial pesticide is defined as

> (A) (A pesticide that) is intended to:
> (i) disinfect, sanitize, reduce or mitigate growth or development of microbiological organisms; or
> (ii) protect inanimate objects, industrial processes or systems, surfaces, water, or other chemical substances from contamination, fouling or deterioration caused by bacteria, viruses, fungi, protozoa, algae, or slime;

With respect to the scope of pests covered by the definition, paragraph (i) focusses on the intended pesticidal function (disinfect, sanitize, etc.) against non-specific "microbiological organisms," while paragraph (ii) focusses on non-specific "protection" provided by the pesticide against specified microorganisms (bacteria, viruses, etc). As a practical matter, EPA believes that the term "microbiological organisms" in paragraph (i) should be considered to include each of the specific types of microorganisms in paragraph (ii) –bacteria, viruses, fungi, protozoa, and algae. Therefore, EPA will consider any product intended for use against the microorganisms specified in paragraph (ii) to be an antimicrobial pesticide (subject to the exclusions discussed in Unit VI.B. and C.)

Having identified the universe of substances that, based upon the intended pesticidal purpose, are antimicrobial pesticides, the definition goes on in paragraphs (1)(B) and (2) to exclude certain pesticides from the definition of antimicrobial pesticide. These exclusions may be characterized as use-based, that is, a pesticide is excluded because of how or where it is used, and not because of the pests or purpose of use.

B. Food Use Exclusion

FIFRA section 2(mm)(1)(B) excludes from "antimicrobial pesticide" those pesticides whose intended antimicrobial use is such that residues in food requiring regulation under section 408 or 409 of the FFDCA might result.

> (B) (A pesticide that) to the intended use is exempt from, or otherwise not subject to, a tolerance under section 408 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 346a and 348) or a food additive regulation under section 409 of such Act.

In creating this exclusion, Congress recognized that applications for registration of food uses that require clearance under FFDCA require extensive data and relatively complex risk assessments that take longer to review. Moreover, obtaining an FFDCA clearance is a formal regulatory procedure. As discussed in Unit VIII.H., FIFRA section 3(h) establishes goals for completion of Agency review of an application for registration. In EPA's view, Congress recognized the difficulty of requiring the review timeframes for registration to encompass the complexities of FFDCA clearance as well. Accordingly, EPA believes that Congress intended the statutory definition to allow exclusion of any antimicrobial pesticide that would require the extensive clearance process of the FFDCA.

The statutory language uses the phrases "exempt from" and "not subject to" a clearance under FFDCA. The phrase "exempt from" is clear and has meaning under FFDCA: an exemption from the requirement of a tolerance is a formal regulatory determination made by EPA. Exemptions from the requirement of a tolerance are found in 40 CFR part 180.

The phrase "not subject to" is not a formal determination under FFDCA. Any product that bears a food use is "subject to" a tolerance, that is, a tolerance or other clearance is required, whether that tolerance has been established or not. EPA believes the statutory language may be unintentionally broad in not differentiating between food uses subject to an "existing" tolerance and those subject to a "new" tolerance. Products and uses subject to an existing tolerance do not require extensive review; only products subject to a new tolerance require such review. As written, the definition excludes both types of antimicrobial pesticides, although the apparent intent is to exclude only those requiring the lengthy and complicated tolerance-setting review associated with a new clearance.

In its discretion, EPA proposes to narrow the food use exclusion to conform to what it believes is the probable intent of Congress. EPA proposes to exclude from the definition of "antimicrobial pesticide" only products bearing one or more uses for which a new clearance is needed, or an amendment of an existing clearance. EPA proposes to include in the definition of "antimicrobial pesticide" (to exclude from the exclusion) product/uses "subject to" an existing tolerance. EPA believes that this narrower policy choice, while not required, more closely reflects the intent to include in the definition of "antimicrobial pesticide" products requiring little or no review and to exclude only products needing the extensive and time-consuming evaluation associated with the establishment of a new or amended clearance.

An antimicrobial pesticide, then, is a product bearing only non-food uses, only food uses covered by an existing clearance under FFDCA, or some combination of these two.

Given the food use exclusion, it is clear that the status of an antimicrobial product as an "antimicrobial pesticide" within the meaning of FIFRA section 3(h) is not necessarily a permanent designation, but may shift according to its intended use. A product could be included or excluded from the definition if the intended use changes. The status of a pesticide as an "antimicrobial pesticide" becomes pertinent and can only be determined at the time of submission of an application for Agency decision. At that time, EPA must determine whether the pesticide application is for an antimicrobial pesticide within the meaning of the statutory definition.

The prime example of this use-dependent phenomenon is an application seeking the first food use of an antimicrobial pesticide. A product that heretofore has been an "antimicrobial pesticide" because it bears only non-food uses or tolerance-covered food uses is no longer an "antimicrobial pesticide" for purposes of EPA review and decision on that first food use action. Provisions of FIFRA applying only to "antimicrobial pesticides," notably the review periods, would not be triggered for that action. Once the food use issue is resolved or a tolerance issued, such that the food use is covered by an existing tolerance, the product may revert to "antimicrobial pesticide" status for a subsequent action.

C. Other Specific Exclusions

FIFRA section 2(mm)(2) contains further specific exclusions to the definition. These are intended to clarify that certain types of products that might be considered "antimicrobial pesticides" because they have a pesticidal effect on the defined types of microorganisms are nonetheless not to be regulated as antimicrobial pesticides for purposes of FIFRA section 3(h). It should be noted that certain types of antimicrobial products are already excluded from regulation under FIFRA, and therefore from any coverage under this proposed rule. Products used against microorganisms in or on man or other living animals are not pesticides because such microorganisms are not "pests" under FIFRA section 2(t). Products intended for use against microorganisms in or on man and animals are regulated solely by FDA. This is not a change from longstanding FIFRA provisions.

1. *Certain wood preservatives and antifouling paints.* Any product that is a wood preservative or antifoulant paint, and that also bears any claim for a pesticidal activity other than or in addition to those specified in section 2(mm)(1) is not an antimicrobial pesticide. The pesticidal activities that generally define an "antimicrobial pesticide" include activity against any microbiological organisms, and "protection" against the destructive effects of bacteria, viruses, fungi, protozoa, algae, and slime.

Both wood preservatives and antifoulant paints (which are used to protect surfaces in contact with water such as boats) may function to protect against bacteria, fungi, etc., and thus, without a specific exclusion, would be deemed to be antimicrobial pesticides. However, since most wood preservatives also protect against insect damage, and most antifouling paints also protect against barnacles, the majority of these products are not likely to be "antimicrobial pesticides." As discussed in Unit VIII.H., however, some wood preservative products may be eligible for the review deadlines that apply to antimicrobial pesticides.

2. *Agricultural fungicides.* The definition of antimicrobial pesticide in FIFRA section 2(mm) excludes "agricultural fungicides." Traditionally, the term "fungus" in an agricultural context has been used to mean microorganisms that are pathogenic to plants. Fungi (and other microorganisms) that are pathogenic to man and animals have historically been treated separately because of their public health implications. However, FIFRA section 2(k) defines "fungus" broadly to include a variety of other microorganisms, including rust, smut, mildew, mold, yeast, and bacteria, without specific reference to whether the microorganisms are pathogenic to plants or to man and animals.

EPA intends the term "agricultural fungicide" to apply to all products applied in or on growing crops or to soil (i.e., pre-harvest application), regardless of the type of pest fungus. Although this would exclude as "antimicrobial pesticides" products applied pre-harvest against microorganisms that might be pathogenic to man and animals, EPA is not aware that any pesticides are currently registered against human and animal pathogens on growing crops. EPA would regulate such products if the need arose, but they would not be covered by subpart W.

Under this interpretation, a product intended for post-harvest application against fungi (including bacteria) would not be an "agricultural fungicide." Significantly, however, such a product would not necessarily be an "antimicrobial pesticide" either, since the food use exclusion also comes into play. Post-harvest application of fungicides or antimicrobial products to food or feed crops would run afoul of the food use exclusion if a new or amended tolerance were needed to cover pesticide residues. All post-harvest use antimicrobial products would be subject to subpart W generally; however, not all would be "antimicrobial pesticides" eligible for the review periods in § 152.457.

3. *Aquatic herbicides.* Further, the definition of antimicrobial pesticide excludes aquatic herbicide products. EPA interprets the term aquatic herbicide to mean pesticides used in or near environmental bodies of water, such as lakes, streams, or ponds, for the control of algae or weeds. In contrast, a

Page 211 contains personal privacy information and is not included in this copy.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAR 22 1989

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

CERTIFIED MAIL

Dear Sir/Madam:

This Notice requires you and other registrants to submit certain data to the U.S. Environmental Protection Agency (EPA) in support of your pesticide products that are registered as antifoulant paints or technical products for the production of antifoulant paints for the purpose of inhibiting the growth of certain aquatic organisms and that contain any of the following organotin compounds as an active ingredient. The subject compounds are bis(tributyltin) oxide, bis(tributyltin) adipate, bis(tributyltin) dodecenyl succinate, bis(tributyltin) sulfide, tributyltin acetate, tributyltin acrylate, tributyltin fluoride, tributyltin methacrylate (and copolymer), tributyltin resinate, and triphenyltin fluoride. These data are necessary to maintain the continued registration of your product(s) containing such active ingredients(s). Within 90 days after you receive this Notice you must respond to this Notice as set forth in section III-A of this Notice. Your response must state:

1. how you will comply with the requirements set forth in this Notice (see section III-A and III-B); or

2. why you believe you are exempt from the requirements of this Notice (see section III-C); or

3. why you believe EPA should not require your submission of data in the manner specified by this Notice (see section III-D).

If you do not respond to this Notice, or if you do not satisfy EPA that you will comply with its requirements, or should be exempt or excused from doing so, then the registration of your product(s) subject to this Notice will be subject to suspension. We have provided a list of all of your products subject to this Notice

III-C. EXEMPTION FROM THE REQUIREMENTS OF THIS NOTICE

Generic Data Exemption - Under section 3(c)(2)(D) of FIFRA, an applicant for registration of a product is exempt from the requirement to submit or cite generic data concerning an active ingredient if the active ingredient in his product is derived exclusively from purchased, registered pesticide products containing the active ingredient. EPA has concluded, as an exercise of its discretion, that it normally will not suspend the registration of a product which would qualify for the generic data exemption in section 3(c)(2)(B) of FIFRA. To qualify, all of the following requirements must be met:

1. The tributyltin compounds in your registered product must be present solely because of incorporation of another registered product which contains tributyltin compounds and is purchased from a source not connected with you;

2. Every registrant who is the ultimate source of the tributyltin compounds in your product must be in compliance with the requirements of this Notice and must remain in compliance; and

3. You must have provided to EPA an accurate and current "Confidential Statement of Formula" for each of your products to which this Notice applies.

A Data Call-In Notice dated January 30, 1987 entitled "Generic Data Exemption Data Call-In Notice" explained the requirements for qualifying for a Generic Data Exemption and offered registrants the opportunity to apply for Generic Data Exemption for any of their product(s) that met the criteria stated in that Notice. If you responded to the January 30, 1987 Notice by applying for a Generic Data Exemption for your product(s) and your product(s) is still eligible for the Generic Data Exemption and your response has not been rejected by EPA, YOU NEED NOT RESPOND TO THIS NOTICE. In such cases the Agency will consider that you now have a Generic Data Exemption from the requirements of the Notice.

If your response to the January 30, 1987 Notice indicated that your product did not qualify for the Generic Data Exemption (or you did not respond to that Notice), but you now consider that your product(s) would qualify, you may request a Generic Data Exemption. To apply for the Generic Data Exemption you must submit a completed " "Generic" Data Exemption Statement" (Attachment E) and all supporting documentation,along with the completed 90-Day Data Call-In Summary Sheet(s), for each of your products for which you claim the exemption.

If you are granted a Generic Data Exemption, you rely on the efforts of other persons to provide the Agency with the required data. If the registrant(s) who have committed to generate and submit the required data fail to take appropriate steps to meet the requirements or are no longer in compliance with this Data Call-In Notice, the Agency will consider that both they and you are not in compliance and will normally initiate proceedings to suspend the registrations of both your and their product(s), unless you commit to submit, and do submit the required data within the specified time. In such cases the Agency generally will not grant a time extension for submitting the data.

Exemption for low volume, minor use pesticides[5] - Section 3(c)(2)(A) of FIFRA requires EPA to consider the appropriateness of requiring data for low volume, minor use pesticides. In implementing this provision EPA considers as low volume pesticides only those active ingredients whose total production volume for all pesticide registrants is small. In determining whether to grant a low volume, minor use waiver the Agency will consider the extent, pattern and volume of use, the economic incentive to conduct the testing, the importance of the pesticide, and the exposure and risk from use of the pesticide. If an active ingredient is used for both high volume and low volume uses, a low volume exemption will not be approved. If all uses of an active ingredient are low volume and the combined volumes for all uses are also low, then an exemption may be granted, depending on review of other information outlined below. An exemption will not be granted if any registrant of the active ingredient elects to conduct the testing. Any registrant receiving a low volume minor use waiver must remain within the sales figures in their forecast supporting the waiver request in order to remain qualified for such waiver. If granted a waiver, a registrant will be required, as a condition of the waiver, to submit annual sales reports. The Agency will respond to requests for waivers in writing.

To apply for a low volume, minor use waiver, you must submit the following information, as applicable to your product(s), as part of your 90-day response to this notice:

1(A). Total company sales (pounds and dollars) of all registered product(s) containing the active ingredient. If applicable to the active ingredient, include foreign sales for those products that are not registered in this country but are applied to sugar (cane or beet), coffee, bananas, cocoa, and other such crops. Present the above information by year for each of the past five years.

---

[5] The exemption for low volume minor use pesticides is not an available option to address any data requirement in this Notice given the risks arising from TBT use and the overall production volume of TBT products.

(B). Provide an estimate of the sales (pounds and dollars) of the active ingredient for each major use site. Present the above information by year for each of the past five years.

2. Total direct production cost of product(s) containing the active ingredient by year for the past five years. Include information on raw material cost, direct labor cost, advertising, sales and marketing, and any other significant costs listed separately.

3. Total indirect production cost (e.g. plant overhead, amortized plant and equipment) charged to product(s) containing the active ingredient by year for the past five years. Exclude all non-recurring costs that were directly related to the active ingredient, such as costs of initial registration and any data development.

4(A). A list of each data requirement for which you seek a waiver. Indicate the type of waiver sought and the estimated cost to you (listed separately for each data requirement and associated test) of conducting the testing needed to fulfill each of these data requirements.

(B). A list of each data requirement for which you are not seeking any waiver and the estimated cost to you (listed separately for each data requirement and associated test) of conducting the testing needed to fulfill each of these data requirements.

5. For each of the next ten years, a year-by-year forecast of company sales (pounds and dollars) of the active ingredient, direct production costs of product(s) containing the active ingredient (following the parameters in item 2 above), indirect production costs of product(s) containing the active ingredient (following the parameters in item 3 above), and costs of data development pertaining to the active ingredient.

6. A description of the importance and unique benefits of the active ingredient to users. Discuss the use patterns and the effectiveness of the active ingredient relative to registered alternative chemicals and non-chemical control strategies. Focus on benefits unique to the active ingredient, providing information that is as quantitative as possible. If you do not have quantitative data upon which to base your estimates, then present the reasoning used to derive your estimates. To assist the Agency in determining the degree of

importance of the active ingredient in terms of its benefits, you should provide information on any of the following factors, as applicable to your product(s): (a) documentation of the usefulness of the active ingredient in Integrated Pest Management, (b) description of the beneficial impacts on the environment of use of the active ingredient, as opposed to its registered alternatives, (c) information on the breakdown of the active ingredient after use and on its persistence in the environment, and (d) description of its usefulness against a pest(s) of public health significance.

Failure to submit sufficient information for the Agency to make a determination regarding a request for a low volume, minor use waiver will result in denial of the request for a waiver.

SECTION III-D. OTHER COURSES OF ACTION UNDER THIS NOTICE

There are four additional options available in responding in 90 days after receipt of this Notice: 1) you may claim that one or more data requirements should not apply to your product, 2) you may amend your registration to delete the uses to which one or more data requirements apply, 3) you may ask for the voluntary cancellation of your registration(s), and/or 4) you may request that EPA use its discretion and not suspend your registration because of your good faith yet unsuccessful efforts to enter into an agreement for a joint data development/cost sharing program.

1. Applicable Data Requirements -- If the Agency determines that the data requirements of this Notice do not apply to your product(s), you will not be required to supply the data pursuant to section 3(c)(2)(B). If you claim on the 90-Day Data Call-In Summary Sheet that the data requirements are not applicable to your product(s), you must submit an explanation of why you believe they do not apply. You should also submit the current label(s) of your product(s) and a copy of the Confidential Statement of Formula of the product(s). If EPA determines that the data are required for your product(s), you must choose another method of meeting the requirements of this Notice within the time provided by this Notice. Within 30 days of your receipt of the Agency's written decision, you must submit a revised Data Call-In Summary Sheet indicating the option chosen.

2. Voluntary Cancellation or Amendment -- You may avoid the requirements of this Notice by eliminating the uses of your product to which the requirement applies. To do so, you may choose either to request voluntary cancellation of your registration(s) or to seek amendment of the registration to delete the appropriate uses. If you wish to amend your registration, you must submit, along with the 90-Day Data Call-In Summary Sheet, a completed application for amendment, a copy of your proposed amended labeling, and all other

Read for Tues. pre-Meeting

Jack
Housenger/DC/USEPA/US
10/21/2004 05:15 PM

To: Andrew Simons/DC/USEPA/US@EPA, Dennis Edwards/DC/USEPA/US@EPA, Marshall Swindell/DC/USEPA/US@EPA, hardy.michael@epa.gov,
cc:
bcc:
Subject: Fw: minor use waiver

As a bit of background for our minor use waiver meeting on tuesday
this is what I sent to Elizabeth earlier
hope this helps
think about this over the weekend so you have something intelligent to contribute at the meeting

Jack E. Housenger, Associate Director
Antimicrobials Division
Office of Pesticide Programs
703-308-8163
Visit: http://www.epa.gov/pesticides/
----- Forwarded by Jack Housenger/DC/USEPA/US on 10/21/2004 05:15 PM -----

Jack
Housenger/DC/USEPA/US
07/28/2004 08:37 AM

To: brown@chemreg.com
cc:
Subject: minor use waiver

Elizabeth, I have checked into your question on a minor use waiver
there is not much guidance yet as we have yet to receive one under PRIA much less for an antimicrobial
there is some general guidance as to what to submit which I have pasted from our website below
my guess is that the guidance will come once we start seeing them
you could be the first
hope this helps
let me know if you have any additional questions

Guidance on Minor Use Waivers

defines minor use

1. Under what circumstances am I eligible for a fee waiver or reduction for an application related to a minor use?

minor use and

The definition of a minor use is provided in Section 2(ll) and includes use where the total US acreage for the crop is less than 300,000 acres; or the use does not provide sufficient economic incentive to support the initial or continuing registration of a pesticide for such use and, for example, the pesticide plays a significant part in managing pest resistance or in an integrated pest management program. If the application meets the statutory definition of minor use and the anticipated revenues from the uses that are the subject of the application would be insufficient to justify imposition of the full application fee, the Administrator may waive or reduce a registration fee.

we should be very clear about how we make this determination or waive all AD products registration waivers as minor uses

2. What information should I include in my request for a fee waiver or reduction for minor uses?

The request should be in writing and including the following information:

- The company name and company number assigned by OPP to the applicant; the official mailing address under FIFRA; the telephone number and e-mail or fax number of the contact person regarding the fee waiver or reduction request.
- A certification signed by a responsible officer that the documentation submitted to support the waiver or reduction request is true, complete, and correct.
- A market analysis that demonstrates the anticipated revenues from the uses that are the subject of the application should be insufficient to justify the imposing of the full application fee.

3. What information should be included in a market analysis for a minor use waiver or reduction request?

The Agency is considering what information is appropriate for making a determination on a request for a minor use waiver or reduction. The Agency currently believes that the applicant should provide a detailed market analysis that demonstrates the anticipated revenue is expected to be insufficient to justify imposition of the full registration fee. In the market analysis, the applicant should to provide information on the anticipated revenue for the next three years based on projected market price and sales volume assumed for the calculation. The applicant should also provide information of the crops and use sites; primary target pests; application rates; and other supporting market information related to product advantage or disadvantages to competing alternatives.

Jack E. Housenger, Associate Director
Antimicrobials Division
Office of Pesticide Programs
703-308-8163
Visit: http://www.epa.gov/pesticides/

Privileged attorney-client communication

Philip Ross/DC/USEPA/US
10/21/2004 05:32 PM

To Jack Housenger/DC/USEPA/US@EPA
cc Andrew Simons/DC/USEPA/US@EPA, Dennis Edwards/DC/USEPA/US@EPA, hardy.michael@epa.gov, Marshall Swindell/DC/USEPA/US@EPA, Richard
bcc
Subject Re: Fw: minor use waiver

Attorney Client Communication
Attorney Work Product
Deliberative
Privileged and Confidential
Do Not Release

Jack et al:

[redacted]

Phil

Jack Housenger/DC/USEPA/US

Jack
Housenger/DC/USEPA/US
10/21/2004 05:15 PM

To Andrew Simons/DC/USEPA/US@EPA, Dennis Edwards/DC/USEPA/US@EPA, Marshall Swindell/DC/USEPA/US@EPA, hardy.michael@epa.gov, Philip Ross/DC/USEPA/US@EPA, Richard Keigwin/DC/USEPA/US@EPA, Tracy Lantz/DC/USEPA/US@EPA
cc
Subject Fw: minor use waiver

As a bit of background for our minor use waiver meeting on tuesday
this is what I sent to Elizabeth earlier
hope this helps
think about this over the weekend so you have something intelligent to contribute at the meeting

Jack E. Housenger, Associate Director
Antimicrobials Division
Office of Pesticide Programs
703-308-8163
Visit: http://www.epa.gov/pesticides/
----- Forwarded by Jack Housenger/DC/USEPA/US on 10/21/2004 05:15 PM -----

Jack
Housenger/DC/USEPA/US
07/28/2004 08:37 AM

To brown@chemteg.com
cc
Subject minor use waiver

Pre application Discussion

Velma Noble
04/13/04 07:31 AM

To: Jacqueline Campbell-McFarlane/DC/USEPA/US@EPA
cc:
Subject: Benzoic Acid - additional information

----- Forwarded by Velma Noble/DC/USEPA/US on 04/13/2004 07:32 AM -----

Elizabeth Brown <brown@chemreg.com>
04/09/2004 12:20 PM

To: Dennis Edwards/DC/USEPA/US@EPA, Velma Noble/DC/USEPA/US@EPA
cc:
Subject: Benzoic Acid - additional information

Dennis and Velma:
As requested, and on behalf of our client (Petro Canada Lubricants), I am providing additional information on the proposed uses of benzoic acid as a material preservative, to assist the Agency in their internal discussions prior to providing the potential registrant direction necessary for compiling and submitting an application for registration. This information must be considered in addition to what previously was provided, not in place of.

In our phone call on April 7, you requested that I provide you with the following:

- draft labeling - draft labeling is attached, for discussion purposes only. The product name has not yet been decided; the name "Additive A" is simply a placeholder at this time.
- CSF - as previously identified, the active will be USP-NF food grade benzoic acid. To be that grade, the product must be a minimum of 99.5% purity. I've attached an example certificate of analysis from one lot of this grade benzoic acid. The nominal likely will be 100% for labeling and CSF purposes, with the appropriate limits.
- how we intend to address the tier 1 data requirements - in addition to the detailed information provided in the earlier background documents, I've attached a table identifying what I believe are the appropriate requirements and how the registrant intends to address each.

I believe that the attached items will suffice for the additional information you requested, but please let me know if anything is needed.

As identified by Dennis during our phone call, the Agency will meet internally again within the next 2-3 weeks and either provide direction by phone call or arrange a presubmission meeting. I'll look forward to hearing back from you on or before April 29. The registrant is anxious to move forward with preparation of an application but appreciates the Agency's willingness to expend time and effort to help ensure that the application can be prepared and then reviewed in the most efficient manner possible for such a well-known and widely approved compound.

Regards,
Elizabeth
<<20040408 Additive A draft labeling.doc>> <<20040408 Data Requirements and how fulfilled.doc>>
<<example COA.pdf>>

Pages 221 through 225 are claimed confidential by the submitter upon submission to the agency and are not included in this copy.

Page 226 contains the identity of the source of product ingredients and is not included in this copy.

MICROL* Preservative
An Antimicrobial Preservative for Industrial Use in Food Grade Lubricating Oils

KEEP OUT OF REACH OF CHILDREN

DANGER

Active ingredient
Benzoic acid 99.93%
Other ingredients (water) 0.07%
Total 100.00%

FIRST AID: Have the product container or label with you when calling a poison control center or doctor, or going for treatment.	
IF IN EYES	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye • Call a poison control center or doctor for treatment advice
IF INHALED	• Move person to fresh air • If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably by mouth, if possible • Call a poison control center or doctor for further treatment advice
IF SWALLOWED	• Immediately call a poison control center or doctor • Do not induce vomiting unless told to do so by a poison control center or doctor • Do not give any liquid to the person. • Do not give anything by mouth to an unconscious person
IF ON SKIN OR CLOTHING	• Take off contaminated clothing • Rinse skin immediately with plenty of water for 15-20 minutes • Call a poison control center or doctor for treatment advice
FOR 24-HOUR EMERGENCY MEDICAL ASSISTANCE, CALL THE NATIONAL POISON CONTROL CENTER 1-800-222-1222	

EPA Reg. No. xxxx-x
EPA Establishment No. xxxxx-xx-x

Net Contents: 100 lb (45.4 kg)

Petro-Canada Lubricants Division
385 Southdown Rd.
Mississauga, Ontario L5J 2Y3 CANADA

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS

CAUTION. Causes irreversible eye injury. Harmful if swallowed. Avoid contact with skin. Do not get in eyes or on clothing. Wear safety glasses or goggles and protective gloves made of butyl rubber, PVC, or neoprene. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum or using tobacco. Remove contaminated clothing and wash before reuse.

ENVIRONMENTAL HAZARDS

Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

DIRECTIONS FOR USE

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling.

MICROL Preservative should be added to the mineral oil component of lubricants compliant with 21 CFR 178.3570 at a maximum level of 1.0%, in order to prevent decomposition and odors in the lubricant caused by microorganisms. MICROL Preservative can be added at any convenient time during the mixing process.

Finished products containing MICROL Preservative may not make public health claims relating to antimicrobial activity without EPA pesticide registration. When incorporated into treated articles, this product does not protect users of any such treated article or others against foodborne or disease causing bacteria, viruses, germs or other disease causing organisms.

This product is compliant with 21 CFR 184.1021.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage and disposal.

Pesticide Storage: Keep product dry during storage.

Pesticide Disposal: Wastes resulting from the use of this product must be disposed of on site or at an approved waste disposal facility.

Container Disposal: Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into application equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by state and local authorities. If drum is contaminated and cannot be reused, dispose of it in the manner required for its liner.

* MICROL is a trademark of Petro Canada

12/1/2004 Draft

Pages 229 through 231 are claimed confidential by the submitter upon submission to the agency and are not included in this copy.

Please read instructions on reverse before completing form

Form Approved, OMB No. 2070-0060, Approval expires 5-31-98

United States
Environmental Protection Agency
Washington, DC 20460

[X] Registration [ ] Amendment [ ] Other	OPP Identifier Number

Application for Pesticide – Section I

1. Company/Product Number (No company number assigned) 82076-R	2. EPA Product Manager Velma Noble	3. Proposed Classification [X] None [ ] Restricted
4. Company/Product (Name) MICROL PRESERVATIVE	PM # 31	
5. Name and Address of Applicant (include ZIP Code) Petro-Canada Specialty Products and Fluids 2489 North Sheridan Way Mississauga, Ontario L5K 1A8 CANADA [ ] *Check if this is a new address*	6. **Expedited Review.** In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to: EPA Reg No. _____ Product Name _____	

Section - II

- [ ] Amendment – Explain below
- [ ] Final printed labels in response to
- [ ] Resubmission in response to Agency letter dated _____
- [ ] Agency letter dated "Me Too" Application
- [ ] Notification – Explain below
- [X] Other – Explain below

Explanation: Use additional page(s) if necessary. (For Section I and Section II.)

Application for registration of new antimicrobial active ingredient.
PRIA Category A38, application fee $90,000. Contact point for fee and invoice: Elizabeth Brown, Agent for Petro-Canada, fax: 703-492-0668, email brown@chemreg.com

COMPANY NUMBER TO BE ASSIGNED.

Section III

1. Material This Product Will be Packaged in:

Child-Resistant Packaging	Unit Packaging		Water Soluble Packaging		2. Type of Container
[ ] Yes [X] No	[ ] Yes [X] No		[ ] Yes [X] No		[ ] Metal [ ] Plastic [ ] Glass [ ] Paper [X] Other (Specify) polyethylene liner in fiberboard drum
Certification must be submitted	If "Yes" Unit Packaging wgt.	No. per container	If "Yes" Package wgt	No. per container	

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of label directions
[X] Label [ ] Container	100 lb (45.4 kg)	[ ] On Label [X] On Label accompanying product

6. Manner in Which Label is Affixed to Product
- [ ] Lithograph
- [X] Paper glued
- [ ] Stenciled
- [ ] Other _____

Section IV

1. Contact Person (*Complete items directly below for identification of individual to be contacted, if necessary, to process this application.*)

Name	Title	Telephone No. (Include Area Code)
Elizabeth Anne Brown	ChemReg International, LLC Authorized agent	703-492-7905

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law

6. Date Application Received (Stamped)

2. Signature	3. Title	4. Typed Name	5. Date
Elizabeth Anne Brown	ChemReg International, LLC Authorized Agent for Petro-Canada	Elizabeth Anne Brown	December 16, 2004

EPA Form 8570-1 (Rev. 8-94) Previous editions are obsolete. White – EPA File Copy (Original) Yellow – Applicant Copy

Page 233 contains the product confidential statement of formula and is not included in this copy.